Jan Delaval

Rush

90572

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Inf rmation Center

Requester's Full Name: Victie Kim Examiner #: 76499 Date: 3/19/03

Art Unit: 1614 Phone Number 305-1675 Serial Number: 07/805249

Mail Box and Bldg/Room Location: 2D01 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): 2 + Sheet attached

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

please, help me on structure search of formula I & its utility, see claim ①

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 = 703-308-4498
jan.delaval@uspto.gov

Use: ① Neurological disorder treatment

Claims 1–16. ex) See claim 2-3. Alzheimer's dx, etc.

② Neuro degeneration (see claim 17).

Claims 17–24

③ Neuro Regeneration (See Claim 25)

Claims 25–32.

④ damaged peripheral Nerve (See claim 33).

Claim 33 - 48

****

STAFF USE ONLY

Searcher: Un	**Type of Search**		**Vendors and cost where applicable**
Searcher Phone #: 4468 (5)	NA Sequence (#)		STN
Searcher Location:	AA Sequence (#)	remote outgrowth	Dialog
Date Searcher Picked Up: 4/1/03 41–48	Structure (#)	✓	Questel/Orbit
Date Completed: 4/15/03	Bibliographic		Dr.Link
Searcher Prep & Review Time:	Litigation		Lexis/Nexis
Clerical Prep Time: 20	Fulltext		Sequence Systems
Online Time: +45	Patent Family		WWW/Internet
	Other		Other (specify)

PTO-1590 (8-01)

BEST AVAILABLE COPY

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L37        51899 S L32,L34,L36
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L39           50 S L38
L40        14064 S L38 FUL
                 SAV TEMP L40 VKIM805/A
L41          115 S L40 AND L32
L42           84 S L32 NOT L41
L43          301 S L40 AND L34
L44          185 S L40 AND L36
L45          336 S L41,L43,L44
                 SAV L45 VKIM805A/A
L46        13728 S L40 NOT L45

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L49          119 S L47 AND L30
L50           53 S L48 AND L30
L51          145 S L49,L50
L52           66 S L47,L48 AND L13-L24,L26-L29
L53          151 S L51,L52
                 E NEURON/CT
                 E E4+ALL
L54         3448 S E2
                 E NEURON/CT
                 E E40+ALL
L55        27528 S E2
                 E NEURON/CT
                 E E25+ALL
L56         1757 S E2
                 E NERVE/CT
                 E E4+ALL
                 E E4+ALL
L57       141350 S E5,E4+NT
                 E E25+ALL
L58        11157 S E7,E8,E6+NT
                 E E21+ALL
                 E E26+ALL
L59         6157 S E9,E8+NT
                 E E15+ALL
L60         4035 S E2+NT
                 E E13+ALL
                 E E16+ALL
L61          498 S E4+NT
                 E NERVE/CT
L62       128433 S E3-E212
L63        11849 S E218 OR E219
L64         1864 S E280
L65        16330 S E308-E358
L66         9082 S E359
L67         8742 S E370-E372
L68          680 S E373
L69       275389 S E390+NT
                 E E308+ALL
L70        27683 S E3+NT
                 E NEUROLOG/CT
                 E E5+ALL
L71        17771 S E2
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                E E3+ALL
L72        332934 S E4+NT
                E E53+ALL
L73        105878 S E3+NT
                E SPINE/CT
                E E3+ALL
                E E3+ALL
L74          3096 S E9+NT
                E E16+ALL
L75         21997 S E4+NT
L76         14129 S E8+NT
                E STROKE/CT
                E E3+ALL
L77          5605 S E2
                E NEURODEGEN/CT
                E E6+ALL
L78          4266 S E2
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                E E6+ALL
L82          7744 S E3+NT OR E9+NT OR E10+NT
                E NERVE GROWTH FACTOR/CT
                E E3+ALL
L83          9410 S E4,E3
                E NERVE GROWTH FACTOR/CT
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                E NEUROTROPHIC FACTOR/CT
L85           124 S E11
                E E6+ALL
L86          4651 S E6-E10,E5+NT
                E E66+ALL
L87         15134 S E3-E5,E2+NT
L88          4516 S E24+NT
L89           740 S GLIAL(L)DERIV?(L)GROWTH FACTOR
L90          1529 S CILIARY(L)NEUROTROPHIC(L)FACTOR
L91          1868 S GLIAL(L)NEUROTROPHIC(L)FACTOR
L92          3617 S BRAIN(L)DERIV?(L)NEUROTROPHIC(L)FACTOR
L93         13895 S NERVE(L)GROWTH FACTOR
L94         10078 S NEUROTROPHIC(L)FACTOR
L95           409 S NEUROTROPIN 3

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L97             1 S NERVE GROWTH FACTOR/CN
                E BRAIN/CN
                E BRAIN DERIVED/CN
L98             1 S E4
L99           260 S BRAIN (L) NEUROTROPHIC(L)(FACTOR OR PEPTIDE OR PROTEIN)
                E GLIAL/CN
L100          194 S GLIAL (L) NEUROTROPHIC(L)(FACTOR OR PEPTIDE OR PROTEIN)
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                E E3+ALL
L103         4099 S E2
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L105        727 S E6
L106       2683 S E8
L107        727 S E14
L108        727 S E18
L109         70 S L53 AND L54-95,L102-L108
L110        197 S L47,L48 AND L54-95,L102-L108
L111        278 S L53,L109,L110
L112         92 S L111 AND (PY<=1995 OR PRY<=1995 OR AY<=1995)
L113         35 S L112 NOT P/DT
L114          7 S L113 AND L6,L25
L115         20 S L113 AND L12
L116         20 S L114,L115
L117         57 S L112 NOT L113
L118         14 S L117 AND L6,L25
L119         21 S L117 AND L12
L120         21 S L118,L119
L121         11 S L112 AND L13-L17
L122          9 S L112 AND L18,L19,L22
L123          8 S L28 AND L111
L124         41 S L116,L120-L123
L125         41 S L124 AND L3-L30,L47-L95,L102-L124
L126         15 S L125 AND (?ALZHEIM? OR ?PARKINSON? OR ?COGNIT? OR DEMENT? OR
L127         26 S L125 NOT L126
L128         11 S L121-L123
L129         11 S L128 AND L126
L130         15 S L126,L129
L131         51 S L112 NOT L124-L130
L132         12 S L131 AND (ALZHEIM? OR PARKINSON?)/CW
L133         25 S L131 AND (BRAIN, DISEASE OR NERVE, DISEASE OR NERVOUS SYSTEM
L134         28 S L132,L133
L135         10 S L134 AND (HIV OR OSTHOL OR CASSETTES OR COLLAGENASE OR CHOLEC
L136         18 S L134 NOT L135
L137         33 S L130,L136
L138         31 S L137 AND (?ALZHEIM? OR ?PARKINSON? OR ?AMYLO? OR TAU OR NEUR?
L139          2 S L137 NOT L138
L140          1 S L139 NOT CYCLOSPORIN
L141         32 S L138,L140

     FILE 'REGISTRY' ENTERED AT 08:15:03 ON 08 APR 2003

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 08:15:13 ON 08 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 8 Apr 2003  VOL 138 ISS 15
FILE LAST UPDATED: 7 Apr 2003  (20030407/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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=> d l141 all fhitstr tot

L141 ANSWER 1 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:332684 HCAPLUS
DN 136:340999
TI Preparation of amino acid derivatives as **rotamase** enzyme activity inhibitors
IN **Steiner, Joseph P.; Hamilton, Gregory S.**
PA USA
SO U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 359,351.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-225
ICS A61K031-16
NCL 514547000
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 15, 63
FAN.CNT 8

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 2002052410	A1	20020502		US 2001-805249	20010314	<--
	US 5614547	A	19970325		US 1995-479436	19950607	<--
	US 2002013344	A1	20020131		US 1995-551026	19951031	<--
	US 6509477	B1	20030121		US 1999-359351	19990721	<--
PRAI	US 1995-479436	A1	19950607	<--			
	US 1995-551026	A2	19951031	<--			
	US 1996-693003	B1	19960806				
	US 1999-359351	A2	19990721				

OS MARPAT 136:340999
AB The invention relates to methods of using **neurotrophic** compds. having an affinity for **FKBP**-type **immunophilins** to stimulate or promote **neuronal** growth or **regeneration** and to prevent **neuronal degeneration**. Amino acid derivs. R1C(:X)CON(J)CHKCO-Y(CH2)nCHZR2 [n = 0-3; Y is CH2, O, NH, or alkylimino; Z and R2 are independently Ar, or cycloalkyl, cycloalkenyl, or Ar-(un)substituted alkyl or alkenyl, or TCH:C(Q)CH2-, where Q = H, alkyl or alkenyl; T is Ar or substituted cycloalkyl; Ar is an (un)substituted mono or bicyclic heterocyclic arom. ring; R1 is U, where U is H, (un)substituted alkyl, alkoxy, alkenyl, alkenyloxy, cycloalkyl or cycloalkenyl; X is O or CH-U , provided that if R1 is H, then X is CH-U or if X is O then R1 is U; J is H, alkyl or benzyl; K is alkyl, benzyl or cyclohexylethyl; or J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain O, S, SO or SO2] or their pharmaceutically acceptable salts are claimed. Thus, 3-(3,4,5-trimethoxyphenyl)propyl (2S)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidinecarboxylate was prepd. by esterification of the acid and showed Ki = 0.025 .mu.M for inhibition of **rotamase** and ED50 = 80 nM for **neurite** outgrowth in chick dorsal root ganglion (DRG) cultures.
ST **FKBP immunophilin rotamase** inhibitor glyoxalylprolinate prepn; prolinate glyoxalyl prepn inhibitor **rotamase**; pipecolinate glyoxalyl prepn inhibitor **rotamase**
IT **Immunophilins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**FKBP** (**FK 506-binding protein**); prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)
IT **Anti-Alzheimer's agents**
Anti-ischemic agents
Antiparkinsonian agents
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as

rotamase inhibitors)

IT **Immunophilins**
Neurotrophic factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT Amino acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **Brain, disease**
(**stroke**; prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 60336-68-7P 76391-12-3P 83079-95-2P 83079-96-3P **141083-86-5P**
141084-02-8P 141084-12-0P 141084-13-1P
141084-14-2P 141084-34-6P 141084-35-7P
141084-39-1P 141084-41-5P 141084-42-6P
141084-63-1P 141097-91-8P 145912-40-9P
145912-57-8P 155404-00-5P **186268-50-8P 186268-51-9P**
186268-52-0P 186268-53-1P 186268-55-3P
186268-56-4P 186268-58-6P 186268-63-3P
186268-69-9P 186452-06-2P 186452-07-3P
186452-08-4P 186452-09-5P 186834-74-2P
186834-75-3P 188614-85-9P 188614-86-0P
188614-93-9P 188614-99-5P 188615-02-3P
188615-03-4P 188615-04-5P 188615-05-6P
188615-14-7P 189328-04-9P 190444-03-2P
205388-68-7P **217308-44-6P** 251949-17-4P 251949-25-4P
252002-68-9P 391669-36-6P 409366-63-8P
409366-64-9P 409366-65-0P 409366-66-1P
409366-67-2P 409366-68-3P 409366-69-4P
409366-70-7P 409366-71-8P 409366-72-9P
409366-73-0P 409366-74-1P 409366-75-2P
409366-76-3P 409366-77-4P 409366-78-5P 409366-79-6P
409366-80-9P 409366-81-0P 409366-82-1P
409366-83-2P 409366-84-3P 409366-85-4P
409366-86-5P 409366-87-6P 409366-88-7P
409366-89-8P 409366-90-1P 409366-91-2P
409366-92-3P 409366-93-4P 409366-94-5P
409366-95-6P 409366-96-7P 409366-97-8P
409366-98-9P 409366-99-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 60-12-8, Benzeneethanol 85-41-6, Phthalimide 86-81-7 91-01-0, Diphenylmethanol 103-63-9 104-53-0, Benzenepropanal 120-57-0, 1,3-Benzodioxole-5-carboxaldehyde 122-97-4, 3-Phenyl-1-propanol 535-75-1, 2-Piperidinecarboxylic acid 677-22-5, tert-Butylmagnesium chloride 2043-61-0, Cyclohexanecarboxaldehyde 2133-40-6, L-Proline methyl ester hydrochloride 2637-34-5, 2-Mercaptopyridine 2859-67-8, 3-(3-Pyridyl)-1-propanol 3277-89-2, Phenethylmagnesium bromide 3360-41-6, 4-Phenyl-1-butanol 3840-31-1, 3,4,5-Trimethoxybenzyl alcohol 5381-92-0, 1,3-Diphenyl-2-propanol 5781-53-3, Methyl oxalyl chloride 6287-38-3 7417-19-8, Benzeneethanol, 2,5-dimethoxy- 10521-91-2, 5-Phenyl-1-pentanol 15862-72-3 17486-86-1, 1,5-Diphenyl-3-pentanol

28276-08-6, 1,1-Dimethylpropylmagnesium chloride 33538-81-7 64439-32-3
69610-41-9 88755-16-2, 3,4,5-Trimethoxybenzoylformic acid 114096-03-6
134804-92-5, 1,7-Diphenyl-4-heptanol 409367-00-6 409367-07-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 1083-30-3P 4407-36-7P 14097-24-6P 20329-96-8P 26429-99-2P
29766-50-5P 30273-62-2P 40918-96-5P 53560-26-2P 58095-76-4P
68889-69-0P 82475-75-0P 89113-44-0P 98303-20-9P **139419-63-9P**
145912-56-7P 148775-22-8P **186268-77-9P** 186268-78-0P
186834-62-8P 194232-16-1P 201991-23-3P 205388-63-2P
409367-01-7P 409367-02-8P 409367-03-9P 409367-04-0P 409367-05-1P
409367-06-2P 409367-08-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

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RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

RN 95076-93-0 HCAPLUS
CN Isomerase, peptidylprolyl cis-trans- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L141 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:276521 HCAPLUS
DN 136:310178
TI Preparation of amino acid derivatives as **rotamase** enzyme activity inhibitors
IN **Steiner, Joseph P.; Hamilton, Gregory S.**
PA USA
SO U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Ser. No. 551,026.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K038-05
ICS A61K031-221; A61K031-16
NCL 514019000
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 15, 63
FAN.CNT 8

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 2002042377	A1	20020411		US 2001-873298	20010605	<--
	US 5614547	A	19970325		US 1995-479436	19950607	<--
	US 2002013344	A1	20020131		US 1995-551026	19951031	<--
	US 6509477	B1	20030121		US 1999-359351	19990721	<--
PRAI	US 1995-479436	A1	19950607	<--			
	US 1995-551026	A2	19951031	<--			
	US 1996-693003	B1	19960806				
	US 1999-359351	A2	19990721				

OS MARPAT 136:310178
AB The invention relates to methods of using **neurotrophic** compds. having an affinity for **FKBP**-type **immunophilins** to stimulate or promote **neuronal** growth or **regeneration** and to prevent **neuronal degeneration**. Amino acid derivs. R1C(:X)CON(J)CHKCO-Y-Z [Y is O, NH, or alkylimino; Z is H, CHL-Ar, alkyl, alkenyl, cycloalkyl, cycloalkenyl or Ar-substituted alkyl or alkenyl, or TCH:C(Q)CH(L)-, where L and Q are H, alkyl or alkenyl; T is Ar or substituted cyclohexyl; Ar is 1- or 2-naphthyl, 2- or 3-furyl, 2-thienyl, 2-, 3- or 4-pyridyl, (un)substituted phenyl; R1 is U, where U

is H, (un)substituted alkyl, alkoxy, alkenyl, alkenyloxy, cycloalkyl or cycloalkenyl; X is O or CH-U , provided that if R1 is H, then X is CH-U or if X is O then R1 is U; J is H, alkyl or benzyl; K is alkyl, benzyl or cyclohexylethyl; or J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain O, S, SO or SO2] or their pharmaceutically acceptable salts are claimed. Thus, 3-(3,4,5-trimethoxyphenyl)propyl (2S)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidinecarboxylate was prepd. by esterification of the acid and showed Ki = 0.025 .mu.M for inhibition of **rotamase** and ED50 = 80 nM for **neurite** outgrowth in chick dorsal root ganglion (DRG) cultures.

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glyoxalylprolinate prepn; prolinate glyoxalyl prepn inhibitor **rotamase**; pipecolinate glyoxalyl prepn inhibitor **rotamase**

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RL: BSU (Biological study, unclassified); BIOL (Biological study)
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Anti-ischemic agents
Antiparkinsonian agents
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

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(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT Amino acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
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(**stroke**; prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

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(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 60336-68-7P 76391-12-3P 83079-95-2P 83079-96-3P **141083-86-5P**
141084-02-8P 141084-12-0P 141084-13-1P
141084-14-2P 141084-34-6P 141084-35-7P
141084-39-1P 141084-41-5P 141084-42-6P
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145912-57-8P 155404-00-5P **186268-50-8P 186268-51-9P**
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186268-56-4P 186268-58-6P 186268-63-3P
186268-69-9P 186452-06-2P 186452-07-3P
186452-08-4P 186452-09-5P 186834-74-2P
186834-75-3P 188614-85-9P 188614-86-0P
188614-93-9P 188614-99-5P 188615-02-3P
188615-03-4P 188615-04-5P 188615-05-6P
188615-14-7P 189328-04-9P 190444-03-2P
205388-68-7P **217308-44-6P** 251949-17-4P 251949-25-4P
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409366-98-9P 409366-99-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 60-12-8, Benzeneethanol 85-41-6, Phthalimide 86-81-7, 3,4,5-Trimethoxybenzaldehyde 91-01-0, Diphenylmethanol 100-52-7, Benzaldehyde, reactions 103-63-9, Phenethyl bromide 104-53-0, Benzenepropanal 122-97-4, 3-Phenyl-1-propanol 535-75-1, 2-Piperidinecarboxylic acid 677-22-5, tert-Butylmagnesium chloride 2133-40-6, L-Proline methyl ester hydrochloride 2637-34-5, 2-Mercaptopyridine 2859-67-8, 3-(3-Pyridyl)-1-propanol 3277-89-2, Phenethylmagnesium bromide 3360-41-6, 4-Phenyl-1-butanol 3840-31-1, 3,4,5-Trimethoxybenzyl alcohol 5381-92-0, 1,3-Diphenyl-2-propanol 5781-53-3, Methyl oxalyl chloride 6287-38-3, 3,4-Dichlorobenzaldehyde 7417-19-8, Benzeneethanol, 2,5-dimethoxy- 10521-91-2, 5-Phenyl-1-pentanol 15862-72-3 17486-86-1, 1,5-Diphenyl-3-pentanol 28276-08-6, 1,1-Dimethylpropylmagnesium chloride 33538-81-7 64439-32-3 69610-41-9 88755-16-2, 3,4,5-Trimethoxybenzoylformic acid 114096-03-6 134804-92-5, 1,7-Diphenyl-4-heptanol 409367-00-6 409367-07-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 1083-30-3P 4407-36-7P 14097-24-6P 20329-96-8P 26429-99-2P 29766-50-5P 30273-62-2P 53560-26-2P 68889-69-0P 82475-75-0P 89113-44-0P 98303-20-9P **139419-63-9P** 145912-56-7P 148775-22-8P **186268-77-9P** 186268-78-0P **186834-62-8P** **194232-16-1P** 201991-23-3P 205388-63-2P 409367-01-7P 409367-02-8P 409367-03-9P 409367-04-0P 409367-05-1P 409367-06-2P 409367-08-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)
RN 95076-93-0 HCAPLUS
CN Isomerase, peptidylprolyl cis-trans- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L141 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:687445 HCAPLUS
DN 135:236450
TI Prolyl ester compound inhibitors of **rotamase** activity, their preparation, and their use
IN **Hamilton, Gregory S.; Steiner, Joseph P.**
PA **GPI NIL Holdings, Inc., USA**
SO U.S., 20 pp., Cont.-in-part of U. S. 693,003.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-401
NCL 514423000
CC 1-11 (Pharmacology)

Section cross-reference(s): 34

FAN.CNT 8

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 6291510	B1	20010918		US 1998-73962	19980507	<--
	US 5614547	A	19970325		US 1995-479436	19950607	<--
PRAI	US 1995-479436	A1	19950607	<--			
	US 1996-693003	A2	19960806				

OS MARPAT 135:236450

AB The invention provides **neurotrophic** compds. having an affinity for **FKBP**-type **immunophilins**, their prepn., and their use as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, and particularly inhibitors of **peptidyl-prolyl isomerase** or **rotamase** enzyme activity. The compds. of the invention may be used in the treatment of **neurol.** disorders, the prevention of **neurodegeneration**, and the promotion of **neuronal regeneration** and growth.

ST prolyl ester deriv prepn **neurotrophic** compd; **neurol** disorder **neurodegeneration** prolyl ester deriv; **neuron regeneration** growth prolyl ester deriv

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506-binding protein**); prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Nerve**
(**degeneration**; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Nervous system**
(**disease**; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Regeneration**, animal
(**nerve**; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT Cytoprotective agents
(**neuroprotectants**; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Axon**
(outgrowth; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Nervous** system agents
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Neurotrophic factors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Nerve**
(**regeneration**; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT 102-04-5P, 1,3-Diphenylpropanone 14097-24-6P, 1,3-Diphenyl-1-propanol 20329-96-8P **186268-77-9P** 186268-78-0P 207444-86-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **186268-50-8P 186268-51-9P 186268-52-0P 186268-53-1P 186268-54-2P 186268-55-3P 186268-56-4P 186268-71-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT 147-85-3D, Proline, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT 4407-36-7P 7031-03-0P, 1,3-Benzodioxole-5-propanol 26429-99-2P 30273-62-2P 40918-96-5P 53560-26-2P 82475-75-0P 101023-16-9P 148775-22-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT 86-81-7 100-52-7, Benzaldehyde, reactions 103-63-9, 2-(Bromoethyl)benzene 122-97-4, 3-Phenyl-1-propanol 2133-40-6, L-Proline methyl ester hydrochloride 2605-67-6 3182-93-2, L-Phenylalanine ethyl ester hydrochloride 5781-53-3, Methyl oxalyl chloride 28276-08-6, 1,1-Dimethylpropylmagnesium chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

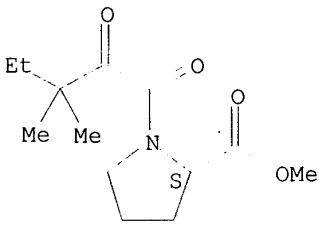
RE

(1) Anon; WO 9641609 1996 HCAPLUS
(2) Armistead; US 5192773 1993 HCAPLUS
(3) Armistead; US 5330993 1994 HCAPLUS
(4) Armistead; US 6037370 2000 HCAPLUS
(5) Birkenshaw; Bioorganic & Medicinal Chemistry Letters 1994, V4(21), P2501
(6) Caffrey; Bioorganic & Medicinal Chemistry Letters 1994, V4(21), P2507 HCAPLUS
(7) Connell; US 5385918 1995 HCAPLUS
(8) Hamilton; US 5614547 1997 HCAPLUS
(9) Hamilton; US 5721256 1998 HCAPLUS
(10) Hamilton; US 5786378 1998 HCAPLUS
(11) Hamilton; US 5795908 1998 HCAPLUS
(12) Hauske; J Med Chem 1992, V35, P4284 HCAPLUS
(13) Holt; Bioorganic & Medical Chemistry Letters 1993, V3(10), P1977 HCAPLUS
(14) Holt; Bioorganic & Medicinal Chemistry Letters 1994, V4(2), P315 HCAPLUS
(15) Holt; J Am Chem Soc 1993, V115, P9925 HCAPLUS
(16) Li; US 5801187 1998 HCAPLUS
(17) Luengo; Bioorganic & Medicinal Chemistry Letters 1994, V4(2), P321 HCAPLUS
(18) Snyder; Nature Medicine 1995, V1(1), P32 HCAPLUS
(19) Steiner; US 5696135 1997 HCAPLUS
(20) Steiner; US 5798355 1998 HCAPLUS
(21) Steiner; US 5801197 1998 HCAPLUS
(22) Stocks; Bioorganic & Medicinal Chemistry Letters 1994, V4(12), P1457 HCAPLUS
(23) Teague; Bioorganic & Medical Chemistry Letters 1994, V4(13), P1581 HCAPLUS
(24) Teague; Bioorganic & Medicinal Chemistry Letters 1993, V3(10), P1947 HCAPLUS
(25) Wang; Bioorganic & Medicinal Chemistry Letters 1994, V4(9), P1161 HCAPLUS
(26) Yamashita; Bioorganic & Medicinal Chemistry Letters 1994, V4(2), P325 HCAPLUS

IT **186268-77-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(prepn. and reaction; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)
RN 186268-77-9 HCAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxopentyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:12270 HCAPLUS
DN 134:80835
TI Reverse-turn mimetics, their preparation, and use in the treatment of cell adhesion-mediated diseases
IN Kahn, Michael; Eguchi, Masakatsu; Kim, Hwa-Ok; Stasiak, Marcin
PA Molecumetics Ltd., USA
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-4985
ICS A61K031-519; C07D487-04; C07D498-04; C07K005-06; A61P009-00; A61P029-00
CC 1-12 (Pharmacology)
Section cross-reference(s): 28, 63
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001000210	A1	20010104	WO 2000-US17053	20000620
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6184223	B1	20010206	US 1999-344221	19990625 <--
	EP 1227813	A1	20020807	EP 2000-941610	20000620
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003503352	T2	20030128	JP 2001-505919	20000620
PRAI	US 1999-344221	A	19990625		
	US 1995-549007	A2	19951027 <--		
	US 1997-846432	A2	19970430		
	WO 2000-US17053	W	20000620		

OS MARPAT 134:80835
AB Conformationally constrained compds. which mimic the secondary structure of reverse-turn regions of biol. active peptides and proteins are disclosed. Such reverse-turn mimetics have utility in the treatment of

cell adhesion-indicated diseases, such as multiple sclerosis, atherosclerosis, asthma and inflammatory bowel disease.

ST reverse turn mimetic prepn cell adhesion disease; multiple sclerosis therapeutic reverse turn mimetic; atherosclerosis asthma therapeutic reverse turn mimetic; inflammatory bowel disease therapeutic reverse turn mimetic

IT AIDS (disease)
(AIDS dementia complex; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT **Mental disorder**
(AIDS dementia; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(LPAM-1 (lymphocyte Peyer's patch high endothelial venule adhesion mol. 1); reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Respiratory distress syndrome
(adult; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Antiarteriosclerotics
(antiatherosclerotics; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Dermatitis
(atopic; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT **Nervous system**
(central, inflammation; reverse-turn mimetic prepn. and use in treatment of **diseases** related to cell adhesion)

IT Drugs
(gastrointestinal; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Intestine, disease
(inflammatory; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Drug delivery systems
(injections, i.v.; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Diabetes mellitus
(insulin-dependent; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Heart, disease
(ischemia; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Antitumor agents
(metastasis; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Kidney, disease
(nephritis; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Secondary structure
(protein, reverse-turn; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Artery, disease
(restenosis; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Eye, disease
(retinitis; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Allergy inhibitors
Analgesics
Anti-AIDS agents

Anti-Alzheimer's agents
Anti-inflammatory agents
Anti-ischemic agents
Antiasthmatics
Antidiabetic agents
Antirheumatic agents
Cardiovascular agents
Cell adhesion
Encephalitis
Meningitis
Psoriasis
(reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT **Brain, disease**
(**stroke**; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Drug delivery systems
(tablets; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Multiple sclerosis
(therapeutic agents; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.4.beta.1; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Opioid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.delta.-opioid; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT Opioid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.mu.-opioid; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT 2032-35-1DP, reaction products with hydroxymethyl polystyrene
86666-85-5P 182121-94-4P 190251-04-8P 215534-57-9P 215534-59-1P
215534-63-7P 215534-65-9P **215534-67-1P** 215534-68-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT 51-67-2 64-04-0, Benzeneethanamine 74-89-5, Methanamine, reactions
141-43-5, reactions 610-30-0, 2,4-Dinitrobenzoic acid 1663-39-4
2032-35-1 2393-23-9 2706-56-1, 2-Pyridineethanamine 3731-51-9,
2-Pyridinemethanamine 6436-90-4, N-Benzylglycine ethyl ester 7252-83-7
9003-53-6D, Polystyrene, hydroxymethyl derivs. 15761-38-3 16640-68-9,
Cyanomethylene triphenylphosphorane 35661-40-6 68858-20-8 92954-90-0
103321-49-9 316792-81-1 316792-82-2 316792-83-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

IT 215533-68-9P 215533-73-6P 215533-78-1P 215533-82-7P 215533-88-3P
215533-94-1P 215534-00-2P 215534-12-6P 215534-16-0P 215534-21-7P
215534-26-2P 215534-31-9P 215534-36-4P 215534-41-1P 215534-46-6P
215534-69-3P 261174-36-1P 261174-41-8P 261174-42-9P 261174-44-1P
316792-30-0P 316792-31-1P 316792-32-2P 316792-33-3P 316792-34-4P
316792-35-5P 316792-36-6P 316792-37-7P 316792-38-8P 316792-39-9P
316792-40-2P 316792-41-3P 316792-42-4P 316792-43-5P 316792-44-6P
316792-45-7P 316792-46-8P 316792-47-9P 316792-48-0P 316792-49-1P
316792-50-4P 316792-51-5P 316792-52-6P 316792-53-7P 316792-54-8P

316792-55-9P 316792-56-0P 316792-57-1P 316792-58-2P 316792-59-3P
316792-60-6P 316792-61-7P 316792-62-8P 316792-63-9P 316792-64-0P
316792-65-1P 316792-66-2P 316792-67-3P 316792-68-4P 316792-69-5P
316792-70-8P 316792-71-9P 316792-72-0P 316792-73-1P 316792-74-2P
316792-75-3P 316792-76-4P 316792-77-5P 316792-78-6P 316792-79-7P
316792-80-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

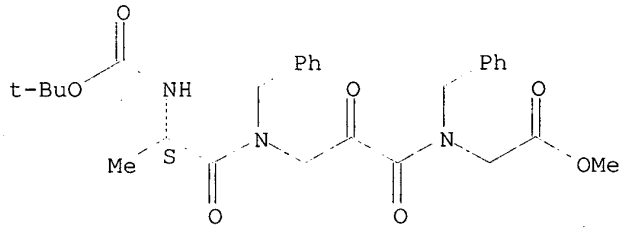
(1) Andrew, J; BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1998, V8, P2297
(2) Boards Of Trustees Of The University Of Illinois; WO 9213878 A 1992 HCAPLUS
(3) David, Y; JOURNAL OF MEDICINAL CHEMISTRY 1997, V40(21), P3359
(4) Molecumetics Ltd; WO 9622304 A 1996 HCAPLUS
(5) Molecumetics Ltd; WO 9630396 A 1996 HCAPLUS
(6) Molecumetics Ltd; WO 9715577 A 1997 HCAPLUS
(7) Molecumetics Ltd; WO 9805333 A 1998 HCAPLUS
(8) Molecumetics Ltd; WO 9849168 A 1998 HCAPLUS
(9) The Board Of Trustees Of The University Of Illinois; WO 9403494 A 1994 HCAPLUS
(10) Thomas, W; JOURNAL OF AMERICAN CHEMICAL SOCIETY 1993, V115(19), P8861

IT **215534-67-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; reverse-turn mimetic prepn. and use in treatment of diseases related to cell adhesion)

RN 215534-67-1 HCAPLUS

CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl-2-oxo-N-(phenylmethyl)-.beta.-alanyl-N-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:732951 HCAPLUS

DN 131:346548

TI Modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids

IN Findeis, Mark A.; Gefter, Malcolm L.; Musso, Gary; Signer, Ethan R.; Wakefield, James; Molineaux, Susan; Chin, Joseph; Lee, Jung-ja; Kelley, Michael; Komar-Panicucci, Sonja; Arico-Muendel, Christopher C.; Phillips, Kathryn; Hayward, Neil J.

PA Praecis Pharmaceuticals, Inc., USA

SO U.S., 40 pp., Cont.-in-part of U.S. Ser. No. 548,998, abandoned.
CODEN: USXXAM

DT Patent

LA English

IC ICM A61K038-06
ICS A61K038-07; A61K038-08; C07K007-06

NCL 424009100
CC 1-11 (Pharmacology)
Section cross-reference(s): 9, 63
FAN.CNT 7

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 5985242	A	19991116		US 1997-920162	19970827	<--
	US 6303567	B1	20011016		US 1996-703675	19960827	<--
	US 6277826	B1	20010821		US 1999-356931	19990719	
	US 2002103134	A1	20020801		US 2001-895443	20010629	<--
PRAI	US 1995-548998	B2	19951027	<--			
	US 1996-616081	B2	19960314				
	US 1996-703675	A	19960827				
	US 1997-897342	B2	19970721				
	US 1995-404831	A2	19950314	<--			
	US 1995-475579	A2	19950607	<--			
	US 1997-920162	A1	19970827				
	US 1999-356931	A1	19990719				

OS MARPAT 131:346548
AB Compds. that modulate natural .beta. **amyloid** peptide aggregation are provided. The modulators of the invention comprise a peptide, preferably based on a .beta. **amyloid** peptide, that is comprised entirely of D-amino acids. Preferably, the peptide comprises 3-5 D-amino acid residues and includes at least two D-amino acid residues independently selected from the group consisting of D-leucine, D-phenylalanine and D-valine. In a particularly preferred embodiment, the peptide is a retro-inverso isomer of a .beta. **amyloid** peptide, preferably a retro-inverso isomer of A.beta.17-21. In certain embodiments, the peptide is modified at the amino-terminus, the carboxy-terminus, or both. Preferred amino-terminal modifying groups include cyclic, heterocyclic, polycyclic and branched alkyl groups. Preferred carboxy-terminal modifying groups include an amide group, an alkyl amide group, an aryl amide group or a hydroxy group. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for **amyloidogenic** diseases using the compds. of the invention, are also disclosed.
ST beta **amyloid** peptide dextro amino acid antiaggregation
IT Molecular association
(aggregation; modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT Drug delivery systems
(carriers; modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT **Cerebrospinal fluid**
(drug stability in; modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT **Brain**
(drug uptake by; modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT **Amyloidosis**
Anti-Alzheimer's agents
Blood-**brain** barrier
Protein sequences
(modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT Toxicity
(**neurotoxicity**; modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT **Amyloid**
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(.beta.-; modulators of .beta.-**amyloid** peptide aggregation

comprising D-amino acids)
IT Amino acids, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(D-; modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT 204333-36-8 204333-38-0 204333-40-4 204333-41-5 204333-59-5
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250370-43-5 250370-49-1 250370-50-4 250386-37-9 250386-38-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT 7440-26-8, Technetium, biological studies 7553-56-2, Iodine, biological studies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(radiolabeling; modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT 134500-80-4 169593-16-2 250599-64-5 250599-65-6 250599-66-7
250599-67-8
RL: PRP (Properties)
(unclaimed protein sequence; modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
IT 145252-42-2 176390-18-4 176390-24-2 182912-78-3 250370-52-6
250370-53-7 250370-54-8 250370-55-9 250370-56-0 250370-57-1
250370-59-3 250370-60-6 250370-61-7 250370-62-8 250370-63-9
250370-64-0 250370-65-1 250370-67-3 250370-68-4 250370-69-5
250370-70-8 250370-71-9 250370-72-0
RL: PRP (Properties)
(unclaimed sequence; modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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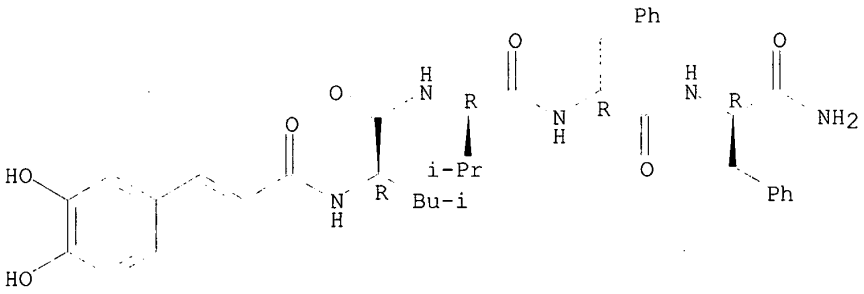
(2) Anon; WO 93/04194 1993 HCAPLUS
(3) Anon; WO 93/11772 1993 HCAPLUS
(4) Anon; EP 641861 1995 HCAPLUS
(5) Anon; EP 681844 1995 HCAPLUS
(6) Harbeson; US 5541290 1996 HCAPLUS
(7) Isowa; US 4119493 1978 HCAPLUS
(8) Potter; US 5338663 1994 HCAPLUS
(9) Roberts; US 5470951 1995 HCAPLUS
(10) Schenk; US 5593846 1997 HCAPLUS
(11) Soto; Biochem Biophys Res Comm 1996, V226, P672 HCAPLUS
IT **204333-68-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(modulators of .beta.-**amyloid** peptide aggregation comprising D-amino acids)
RN 204333-68-6 HCAPLUS
CN D-Phenylalaninamide, N-[3-(3,4-dihydroxyphenyl)-1-oxo-2-propenyl]-D-leucyl-D-valyl-D-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L141 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:45148 HCAPLUS
DN 130:110640
TI Preparation of proline derivatives as inhibitors of **rotamase** enzyme activity
IN **Hamilton, Gregory S.; Steiner, Joseph P.**
PA **GPI NIL Holdings, Inc., USA**
SO U.S., 27 pp., Cont.-in-part of U.S. 5,614,547.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-40
ICS C07D207-16
NCL 514343000
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5859031	A	19990112	US 1996-650461	19960521	<--
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	CA 2206799	AA	19961219	CA 1996-2206799	19960605	<--
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	AU 9661062	A1	19961230	AU 1996-61062	19960605	<--
	AU 703118	B2	19990318			
	GB 2305176	A1	19970402	GB 1996-24257	19960605	<--
	GB 2305176	B2	19991222			
	EP 769006	A1	19970423	EP 1996-918384	19960605	<--
	EP 769006	B1	20001108			
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	DE 19680256	T	19970619	DE 1996-19680256	19960605	<--
	CH 688775	A	19980313	CH 1996-2790	19960605	<--
	CN 1187188	A	19980708	CN 1996-194554	19960605	<--

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	GB 2324527	B2	19991222		
	GB 2325230	A1	19981118	GB 1998-17938	19960605 <--
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	ES 2131457	A1	19990716	ES 1996-50030	19960605 <--
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	JP 2000503626	T2	20000328	JP 1997-501958	19960605 <--
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	JP 2000169444	A2	20000620	JP 1999-235727	19960605 <--
	JP 2000204048	A2	20000725	JP 1999-43437	19960605 <--
	EE 200000317	A	20010615	EE 2000-200000317	19960605 <--
	TW 453992	B	20010911	TW 1996-85113067	19961024
	ZA 9608984	A	19980625	ZA 1996-8984	19961025 <--
	ZA 9608983	A	19980727	ZA 1996-8983	19961025
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	LT 4484	B	19990325	LT 1998-1	19980106 <--
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	AU 733685	B2	20010524		
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	DK 9901519	A	19991022	DK 1999-1519	19991022 <--
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	JP 1997-501958	A3	19960605		
	WO 1996-US9701	W	19960605		
	US 1997-833629	A1	19970408		

OS MARPAT 130:110640

AB **Neurotrophic** N-glyoxyl prolyl esters R1COC(:X)-L-Pro-O-Z [R1 = alkyl or alkenyl optionally substituted by cycloalkyl or aryl groups; X = O, S; Z = (un)substituted alkyl or alkenyl], which have an affinity for **FKBP**-type **immunophilins**, were prepd. for use as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, in particular **peptidyl-prolyl isomerase** (**rotamase**) enzyme activity. Thus, 3-phenylpropyl (2S)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidinecarboxylate was prepd. and showed apparent Ki value 42 for inhibition of **rotamase** activity.

ST glyoxylproline ester prepn inhibitor **rotamase**; proline glyoxyl prepn inhibitor **rotamase**

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506-binding protein**); prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP-12** (**FK 506-binding protein, 12,000-**

mol.-wt.); prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Nervous system**
(amyotrophic lateral sclerosis; prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Nerve**
(**degeneration**; prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Nervous system**
(**disease**; prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Nerve, disease**
(**peripheral neuropathy**; prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Alzheimer's disease**
Parkinson's disease
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Growth factors**, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Immunophilins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **186268-50-8P 186268-51-9P 186268-52-0P**
186268-53-1P 186268-54-2P 186268-56-4P
186268-57-5P 186268-58-6P 186268-63-3P
186268-64-4P 186268-65-5P 186268-66-6P
186268-67-7P 186268-68-8P 186452-05-1P
186452-06-2P 186452-07-3P 186452-08-4P
186452-09-5P 186452-10-8P 186452-11-9P
186452-12-0P 186452-13-1P 186452-14-2P
186452-15-3P 186452-16-4P 186452-17-5P
186452-18-6P 186452-19-7P 186452-20-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT 86-81-7, 3,4,5-Trimethoxybenzaldehyde 122-97-4, 3-Phenyl-1-propanol 5781-53-3, Methyl oxalyl chloride 28276-08-6, 1,1-Dimethylpropylmagnesium chloride 79397-50-5, Proline methyl ester hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT 20329-96-8P, trans-Methyl 3,4,5-trimethoxycinnamate 30273-62-2P 53560-26-2P **139419-63-9P 186268-77-9P** 186268-78-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
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(2) Anon; EP 48159 1982 HCAPLUS
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(4) Anon; EP 88350 1983 HCAPLUS
(5) Anon; EP 196841 1986 HCAPLUS
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(8) Anon; EP 333174 1989 HCAPLUS
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(28) Anon; WO 9219745 1992 HCAPLUS
(29) Anon; WO 9221313 1992 HCAPLUS
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(31) Anon; EP 572365 1993 HCAPLUS
(32) Anon; ZA 9207782 1993 HCAPLUS
(33) Anon; WO 9307269 1993 HCAPLUS
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(35) Anon; WO 9323548 1993 HCAPLUS
(36) Anon; WO 9325546 1993 HCAPLUS
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(39) Anon; WO 9413629 1994 HCAPLUS
(40) Anon; EP 652229 1995 HCAPLUS
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(42) Anon; WO 9524385 1995 HCAPLUS
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(52) Armistead; US 5192773 1993 HCAPLUS
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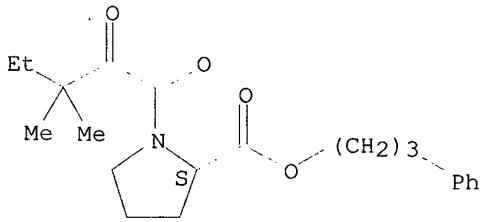
(76) Zelle; US 5543423 1996 HCAPLUS

IT **186268-50-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)
RN 186268-50-8 HCAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxopentyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:599365 HCAPLUS
DN 129:198015
TI **Rotamase** enzyme activity inhibitors
IN **Steiner, Joseph P.; Hamilton, Gregory S.**
PA **GPI Nil Holdings, Inc., USA**
SO U.S., 16 pp., Cont.-in-part of U. S. Ser. No. 551,026, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-445
ICS A61K031-40; A61K031-22; A61K031-24
NCL 514548000
CC 1-11 (Pharmacology)
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5801197	A	19980901	US 1996-645149	19960513 <--
	US 2002013344	A1	20020131	US 1995-551026	19951031 <--
	CA 2236328	AA	19970509	CA 1996-2236328	19960826 <--
	WO 9716190	A1	19970509	WO 1996-US13624	19960826 <--

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KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN
AU 9668573 A1 19970522 AU 1996-68573 19960826 <--
AU 713302 B2 19991125
EP 859614 A1 19980826 EP 1996-929014 19960826 <--
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IE, SI, LT, FI
CN 1205635 A 19990120 CN 1996-199127 19960826 <--
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NO 9801903 A 19980630 NO 1998-1903 19980427 <--
LV 12102 B 19981020 LV 1998-85 19980625 <--
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OS MARPAT 129:198015
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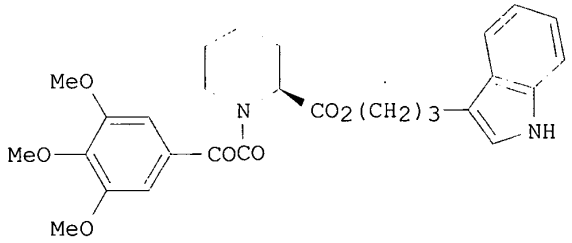

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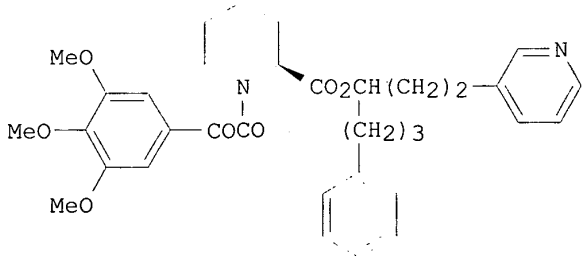

II

AB This invention relates to the method of using specially formulated **neurotrophic** pipecolic acid deriv. compds. having an affinity for **FKBP**-type **immunophilins** as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, and particularly inhibitors of **peptidyl-prolyl isomerase** or **rotamase** enzyme activity to stimulate or promote **neuronal** growth or **regeneration**. The stimulation of **neurite** outgrowth induced by a 300pM dose of I and 1 nM dose of II were demonstrated.

ST **rotamase** enzyme inhibitor pyrrolidinecarboxylate; **neurotrophic** pipecolic acid deriv

IT **Proteins, specific or class**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**FKBP** (**FK 506-binding**

protein); **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

IT **Immunophilins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**FKBP**-type; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

IT **Nervous system**
(amyotrophic lateral sclerosis; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

IT **Nerve**
(**neuron**, growth of; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

IT Structure-activity relationship
(**rotamase** inhibiting; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

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145912-40-9 186834-74-2 186834-75-3
188614-85-9 188614-86-0 188614-93-9
188614-99-5 188615-02-3 188615-03-4
188615-04-5 188615-05-6 188615-14-7
190444-03-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

RE.CNT 173 THERE ARE 173 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)
RN 95076-93-0 HCAPLUS
CN Isomerase, peptidylprolyl cis-trans- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L141 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:163613 HCAPLUS
DN 128:217639
TI Preparation of D-amino acid peptides as modulators of .beta.-**amyloid** peptide aggregation
IN Findeis, Mark A.; Gefter, Malcolm L.; Musso, Gary; Signer, Ethan R.; Wakefield, James; Molineaux, Susan; Chin, Joseph; Lee, Jung-Ja; Kelley, Michael; Komar-Panicucci, Sonja; Arico-Muendel, Christopher C.; Phillips, Kathryn; Hayward, Neil J.
PA Praecis Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-47
ICS A61K038-17; G01N033-68
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
FAN.CNT 7

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9808868	A1	19980305	WO 1997-US15166	19970827
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6303567	B1	20011016	US 1996-703675	19960827 <--

AU 9742387 A1 19980319 AU 1997-42387 19970827
AU 741199 B2 20011122
EP 929574 A1 19990721 EP 1997-940663 19970827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2001500852 T2 20010123 JP 1998-511914 19970827
PRAI US 1996-703675 A 19960827
US 1997-897342 A 19970721
US 1995-404831 A2 19950314 <--
US 1995-475579 A2 19950607 <--
US 1995-548998 B2 19951027 <--
US 1996-616081 B2 19960314
WO 1997-US15166 W 19970827
OS MARPAT 128:217639

AB Compds. that modulate natural .beta.-**amyloid** peptide aggregation are provided. The modulators of the invention comprise a peptide, preferably based on a .beta.-**amyloid** peptide, that is comprised entirely of D-amino acids. Preferably, the peptide comprises 3-5 D-amino acid residues and includes at least two D-amino acid residues independently selected from the group consisting of D-Leu, D-Phe, and D-Val. In a particularly preferred embodiment, the peptide is a retro-inverso isomer of a .beta.-**amyloid** peptide, preferably a retro-inverso isomer of A.beta.17-21. In certain embodiments, the peptide is modified at the amino-terminus, the carboxy-terminus, or both. Preferred amino-terminal modifying groups include cyclic, heterocyclic, polycyclic and branched alkyl groups. Preferred carboxy-terminal modifying groups include an amide group, an alkylamide group, an arylamide group or a hydroxy group. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for **amyloidogenic** diseases using the compds. of the invention, are also disclosed. Thus, peptide H-D-Leu-D-Val-D-Phe-D-Phe-D-Ala-NH2, prepd. by std. solid-phase methods, inhibited aggregation of natural .beta.-**amyloid** peptide with a change in lag time of 3.5 at a concn. of 3 .mu.M.

ST retro inverso peptide enantiomer **Alzheimer** treatment; **amyloid** peptide enantiomer prepn aggregation modulator

IT **Alzheimer's disease**
(prepn. of D-amino acid peptides as modulators of .beta.-**amyloid** peptide aggregation)

IT **Amyloid**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(.beta.-; prepn. of D-amino acid peptides as modulators of .beta.-**amyloid** peptide aggregation)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(D-amino acid-contg.; prepn. of D-amino acid peptides as modulators of .beta.-**amyloid** peptide aggregation)

IT 26305-03-3P, PPI 516 183746-91-0P 204333-36-8P 204333-37-9P
204333-38-0P 204333-39-1P 204333-40-4P 204333-41-5P 204333-42-6P
204333-43-7P 204333-44-8P 204333-45-9P 204333-46-0P 204333-47-1P
204333-48-2P 204333-49-3P 204333-50-6P 204333-51-7P 204333-52-8P
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204333-81-3P 204333-82-4P 204333-83-5P 204333-84-6P 204333-85-7P
204333-86-8P 204333-87-9P 204333-88-0P 204333-89-1P 204333-90-4P
204333-91-5P 204333-92-6P 204333-93-7P

204333-94-8P **204333-95-9P** 204333-96-0P 204333-97-1P
204333-98-2P **204333-99-3P** 204334-00-9P 204334-01-0P
204334-02-1P **204334-03-2P** 204334-04-3P 204334-05-4P
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204334-35-0P 204334-37-2P 204334-39-4P 204334-41-8P 204334-42-9P
204334-43-0P 204334-44-1P 204334-45-2P 204334-46-3P 204334-47-4P
204334-48-5P 204334-49-6P 204334-50-9P 204334-52-1P 204334-54-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of D-amino acid peptides as modulators of .beta.-**amyloid** peptide aggregation)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Flood, E; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA 1994, V91, P380
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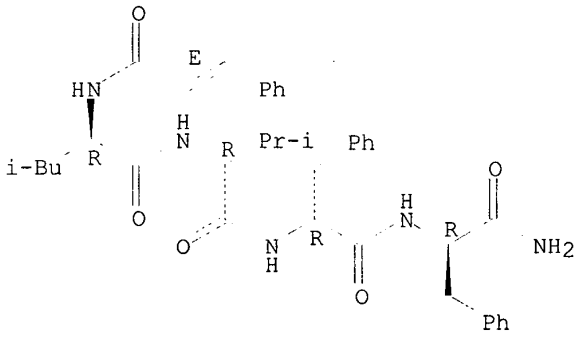
IT **204333-67-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of D-amino acid peptides as modulators of .beta.-**amyloid** peptide aggregation)

RN 204333-67-5 HCAPLUS
CN D-Phenylalaninamide, N-[(2E)-1-oxo-3-phenyl-2-propenyl]-D-leucyl-D-valyl-D-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L141 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:17977 HCAPLUS
DN 128:70783
TI Pipecolic acid derivative inhibitors of **rotamase** enzyme activity effective at stimulating **neuronal** growth

IN **Steiner, Joseph P.**; Snyder, Solomon; **Hamilton, Gregory S.**
PA **GPI NIL Holdings, Inc., USA**; Johns Hopkins Univ. School of Medicines
SO U.S., 47 pp., Cont.-in-part of U.S. Ser. No. 474,072.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-445
ICS A61K038-18
NCL 514317000
CC 1-11 (Pharmacology)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5696135	A	19971209	US 1996-653905	19960528	<--
	US 5798355	A	19980825	US 1995-474072	19950607	<--
	CA 2206824	AA	19961219	CA 1996-2206824	19960605	<--
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	WO 9640140	A1	19961219	WO 1996-US9561	19960605	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	AU 9661622	A1	19961230	AU 1996-61622	19960605	<--
	AU 710423	B2	19990923			
	GB 2305605	A1	19970416	GB 1996-24258	19960605	<--
	GB 2305605	B2	20000112			
	DE 19680255	T	19970605	DE 1996-19680255	19960605	<--
	EP 777478	A1	19970611	EP 1996-919227	19960605	<--
	EP 777478	B1	20011107			
	R: BE, FR, GR, IE, IT, MC, NL					
	CN 1187127	A	19980708	CN 1996-194555	19960605	<--
	CH 689541	A	19990615	CH 1996-2789	19960605	<--
	BR 9608485	A	19990706	BR 1996-8485	19960605	<--
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	ES 2138518	B1	20010101			
	NZ 310767	A	20001124	NZ 1996-310767	19960605	<--
	ES 2166740	A1	20020416	ES 2000-200050035	19960605	<--
	FI 9604137	A	19970115	FI 1996-4137	19961015	<--
	ZA 9608981	A	19980525	ZA 1996-8981	19961025	
	SE 9604097	A	19961208	SE 1996-4097	19961108	<--
	DK 9601256	A	19961220	DK 1996-1256	19961108	<--
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	US 5846981	A	19981208	US 1997-787163	19970123	<--
	NO 9704290	A	19971204	NO 1997-4290	19970917	<--
	LT 4516	B	19990625	LT 1998-2	19980106	<--
	LV 11986	B	19980920	LV 1997-244	19980202	<--
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	AU 9948793	A1	19991125	AU 1999-48793	19990916	<--
	AU 740089	B2	20011101			
	US 2002052372	A1	20020502	US 1999-435323	19991105	<--
PRAI	US 1995-474072	A2	19950607	<--		
	US 1996-653905	A	19960528			
	AU 1996-61622	A3	19960605			
	WO 1996-US9561	W	19960605			
	US 1997-787162	A1	19970123			
	US 1998-113330	A1	19980710			

AB A method is disclosed for using **neurotrophic** pipecolic acid deriv. compds. having an affinity for **FKBP**-type **immunophilins** as inhibitors of the enzyme activity assocd. with

immunophilin proteins, and particularly inhibitors of **peptidyl-prolyl isomerase** or **rotamase** enzyme activity to stimulate or promote **neuronal** growth or **regeneration**. The compds. of the invention are useful for treatment of **neurol**. disorders.

ST **neuron** growth pipecolate deriv **rotamase** inhibitor; **regeneration neuron** pipecolate deriv **rotamase** inhibitor; **neurol** disorder pipecolate deriv **rotamase** inhibitor

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506-binding protein**); pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT mRNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** and GAP-43; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP-12** (**FK 506-binding protein, 12,000-mol.-wt.**); pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT Biological transport
(**FKBP**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT Animal cell line
(PC12; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Nervous system**
(amyotrophic lateral sclerosis; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Neurotrophic factors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**brain-derived**; pipecolic acid **deriv**. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders, and use with **neurotrophic factors**)

IT **Nerve**
(**degeneration**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Nervous system**
(**disease**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**.

disorders)

IT **Nerve**
(**facial**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Neurotrophic factors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glial**-derived; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders, and use with **neurotrophic factors**)

IT **Brain, disease**
Spinal cord
(**injury**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Growth factors**, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**neurite** extension factors; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Nerve**
(**neuron**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Nerve, disease**
(**peripheral neuropathy**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Nerve, disease**
(**peripheral, injury**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Alzheimer's disease**
Nervous system agents
Parkinson's disease
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT GAP-43 (protein)
Immunophilins
Myelin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)

IT **Ciliary neurotrophic factor**
Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders, and use with **neurotrophic factors**)

IT **Nerve**

(**sciatic**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol.** disorders)

IT **Ganglion**
(**spinal**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol.** disorders)

IT **Brain, disease**
(**stroke, brain** damage-assocd.; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol.** disorders)

IT 104987-11-3
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol.** disorders)

IT **9061-61-4, Nerve growth factor**
53123-88-9, Rapamycin 59865-13-3, Cyclosporin A 149438-31-3, WAY-124466
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol.** disorders)

IT 535-75-1D, Pipecolic acid, derivs. **141084-63-1**
152754-33-1 152754-34-2 152754-35-3
152754-36-4 152754-42-2 **155668-86-3** 157757-22-7
186834-66-2 186834-69-5 186834-70-8
186834-71-9 186834-72-0 186834-73-1
186834-74-2 186834-75-3 186834-76-4
186834-77-5 186834-78-6 186834-79-7
186834-80-0 186834-81-1 186834-82-2
186834-83-3 186834-84-4 186834-85-5
186834-86-6 186834-87-7 186834-88-8
200417-73-8 200728-03-6 200728-04-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol.** disorders)

IT 9025-75-6, Calcineurin **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol.** disorders)

IT **130939-66-1, Neurotrophin** 3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and **regeneration** and treating **neurol.** disorders, and use with **neurotrophic factors**)

IT **9061-61-4, Nerve growth factor**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity

for stimulating **neuronal** growth and **regeneration** and treating **neurol**. disorders)
RN 9061-61-4 HCAPLUS
CN Nerve growth factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L141 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:506946 HCAPLUS
DN 127:136081
TI Compounds with growth hormone releasing properties
IN Hansen, Thomas Kruse; Peschke, Bernd; Lau, Jesper; Lundt, Behrend Friedrich; Ankersen, Michael; Watson, Brett; Madsen, Kjeld
PA Novo Nordisk A/s, Den.; Hansen, Thomas Kruse; Peschke, Bernd; Lau, Jesper; Lundt, Behrend Friedrich; Ankersen, Michael; Watson, Brett; Madsen, Kjeld
SO PCT Int. Appl., 528 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-60
ICS C07K005-10; C07K007-02; A61K038-07; A61K038-08
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9723508	A1	19970703	WO 1996-DK529	19961216	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	CA 2239711	AA	19970703	CA 1996-2239711	19961216	<--
	AU 9710929	A1	19970717	AU 1997-10929	19961216	<--
	AU 715856	B2	20000210			
	EP 869974	A1	19981014	EP 1996-941591	19961216	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 11501054	T2	19990126	JP 1996-523230	19961216	<--
	CN 1211991	A	19990324	CN 1996-199770	19961216	<--
	BR 9612275	A	19990713	BR 1996-12275	19961216	<--
	JP 11209336	A2	19990803	JP 1998-247935	19961216	<--
	JP 3007613	B2	20000207			
	JP 2000143613	A2	20000526	JP 1999-328929	19961216	<--
	ZA 9610775	A	19970708	ZA 1996-10775	19961222	<--
	TW 480248	B	20020321	TW 1997-86100130	19970108	<--
	NO 9802872	A	19980821	NO 1998-2872	19980619	<--
PRAI	DK 1995-1462	A	19951222	<--		
	DK 1996-698	A	19960625			
	DK 1996-812	A	19960724			
	DK 1996-1248	A	19961106			
	JP 1996-523230	A	19961216			
	JP 1997-523230	A3	19961216			
	WO 1996-DK529	W	19961216			

OS MARPAT 127:136081
AB Peptide mimetics RCOR1CH[(CH2)mR3]CONR2CHR4(CH2)nR5 [R = ring-substituted alkyl, R1, R2 = H, alkyl, aryl; R3 = (un)substituted alkoxy or aryl; R4 = (un)substituted carbamoyl, alkyl, or aryl; R5 = H, (un)substituted alkoxy or aryl; m, n = 1 or 2] were prepd. as drugs for stimulating the release of growth hormone. Thus, (2E)-5-amino-5-methyl-2-hexenoic acid

N-methyl-N-[(1R)-1-[N-methyl-N-[(1R)-1-(methylcarbamoyl)-2-phenylethyl]carbamoyl]-2-(2-naphthyl)ethyl]amide was prepd. via amidation of the N-protected acid.

ST peptide mimetic prepn simulation growth hormone

IT Disease, animal
(Noonan syndrome; prepn. of peptides with growth hormone releasing properties)

IT **Mental disorder**
(depression; prepn. of peptides with growth hormone releasing properties)

IT Kidney, disease
(failure; prepn. of peptides with growth hormone releasing properties)

IT **Alzheimer's disease**
Cushing's syndrome
Immune system
Osteoporosis
Schizophrenia
Wound healing
(prepn. of peptides with growth hormone releasing properties)

IT Glucocorticoids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of peptides with growth hormone releasing properties)

IT Peptides, preparation
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides with growth hormone releasing properties)

IT 9002-72-6, Growth hormone
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of peptides with growth hormone releasing properties)

IT 109-85-3, 2-Methoxyethylamine 156-87-6 500-99-2 623-73-4, Ethyl diazoacetate 625-03-6 753-90-2, 2,2,2,-Trifluoroethylamine 765-30-0, Cyclopropylamine 867-13-0, Triethyl phosphonoacetate 1099-45-2, Carbethoxymethylenetriphenylphosphorane 1776-53-0 2021-58-1, 2-Thienylalanine 2516-47-4, Cyclopropylmethylamine 2799-17-9 4795-29-3 6136-68-1, 3-Acetylbenzonitrile 14660-52-7 22059-22-9, Acetamidoxime 25462-85-5 36476-78-5, 3-Azetidinecarboxylic acid 41979-39-9, 4-Piperidone hydrochloride 47173-80-8 56601-42-4, Cyclopropyl isothiocyanate 57292-45-2 69610-40-8 76932-48-4 82911-69-1 84000-15-7 85466-66-6 102520-97-8 111082-76-9 111819-71-7 114873-10-8 117445-22-4 128779-47-5 129765-95-3 138775-05-0 147577-61-5 157634-00-9 170080-13-4 179385-30-9 186840-98-2 **193085-20-0** 193085-32-4 193085-44-8 193085-74-4 193086-13-4 193086-15-6 **193086-25-8** 193086-27-0 193086-28-1 193086-30-5 193086-65-6 193086-68-9 193086-70-3 193086-73-6 193086-74-7 193150-14-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of peptides with growth hormone releasing properties)

IT 14719-37-0P 22080-96-2P 79099-07-3P 102339-81-1P 109384-19-2P 115109-57-4P 115109-59-6P 130309-46-5P 133466-99-6P 135216-08-9P 135716-08-4P 142253-55-2P 142253-56-3P 161948-70-5P 165949-84-8P 177947-96-5P 181646-38-8P 181646-40-2P 181646-42-4P 181646-44-6P 181646-45-7P 181646-46-8P 181646-48-0P 181646-55-9P 181646-56-0P 181646-57-1P 183059-24-7P 186840-95-9P 193085-18-6P 193085-19-7P 193085-21-1P 193085-22-2P **193085-23-3P** 193085-24-4P 193085-25-5P 193085-26-6P 193085-27-7P 193085-28-8P 193085-29-9P 193085-30-2P 193085-34-6P 193085-35-7P **193085-37-9P** 193085-38-0P 193085-39-1P 193085-40-4P **193085-41-5P** 193085-42-6P 193085-46-0P 193085-48-2P 193085-49-3P 193085-50-6P 193085-51-7P 193085-52-8P 193085-54-0P 193085-55-1P 193085-56-2P 193085-57-3P 193085-58-4P **193085-59-5P** 193085-60-8P 193085-61-9P 193085-62-0P 193085-63-1P **193085-64-2P** **193085-65-3P** 193085-66-4P 193085-67-5P 193085-68-6P

193085-69-7P 193085-70-0P 193085-71-1P **193085-72-2P**
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193085-90-4P 193085-91-5P **193085-92-6P** 193085-93-7P
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193086-03-2P 193086-04-3P **193086-05-4P** 193086-06-5P
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193086-18-9P 193086-19-0P 193086-20-3P 193086-21-4P 193086-22-5P
193086-23-6P **193086-24-7P** 193086-26-9DP, resin-bound
193086-29-2P 193086-31-6P 193086-32-7P 193086-33-8P 193086-34-9P
193086-36-1P 193086-40-7P 193086-42-9P 193086-43-0P
193086-46-3P 193086-47-4P 193086-48-5P **193086-49-6P**
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193086-55-4P 193086-56-5P 193086-57-6P 193086-58-7P
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193086-64-5P **193087-04-6P** 193150-11-7P 193150-12-8P
193150-13-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptides with growth hormone releasing properties)

IT **193079-29-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of peptides with growth hormone releasing properties)

IT 167216-22-0P 170853-30-2P **193079-01-5P 193079-03-7P**
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193079-11-7P 193079-12-8P 193079-13-9P **193079-14-0P**
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193079-25-3P **193079-26-4P** 193079-27-5P **193079-28-6P**
193079-30-0P 193079-31-1P 193079-32-2P
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193079-38-8P 193079-39-9P 193079-40-2P
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193079-64-0P 193079-65-1P 193079-66-2P
193079-67-3P **193079-68-4P 193079-69-5P**
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193080-82-9P 193080-83-0P **193080-84-1P** 193080-85-2P
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193080-90-9P 193080-91-0P 193080-92-1P 193080-93-2P
193080-94-3P 193080-95-4P 193080-96-5P **193080-97-6P**
193080-98-7P 193080-99-8P 193081-00-4P **193081-01-5P**
193081-02-6P 193081-03-7P **193081-04-8P** 193081-05-9P
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193081-36-6P **193081-37-7P** **193081-38-8P** 193081-39-9P
193081-40-2P **193081-41-3P** **193081-42-4P** 193081-43-5P
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193081-52-6P **193081-53-7P** **193081-54-8P** 193081-55-9P
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193081-73-1P **193081-74-2P** **193081-75-3P** 193081-76-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides with growth hormone releasing properties)

IT 193081-77-5P **193081-78-6P** **193081-79-7P** 193081-80-0P
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RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides with growth hormone releasing properties)

IT 193084-52-5P **193084-53-6P 193084-54-7P**
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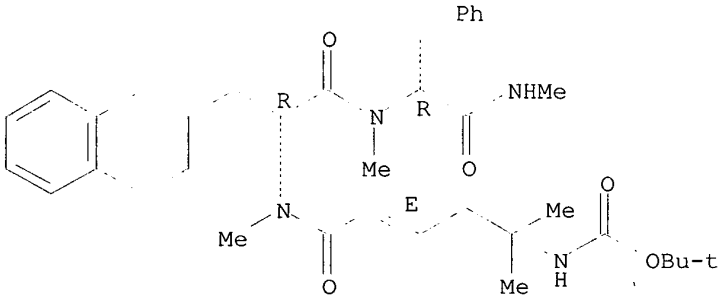
193086-98-5P 193087-00-2P 193087-03-5P
193150-10-6P 193150-15-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides with growth hormone releasing properties)

IT **193085-20-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of peptides with growth hormone releasing properties)

RN 193085-20-0 HCAPLUS
CN D-Phenylalaninamide, N-[(2E)-5-[[(1,1-dimethylethoxy)carbonyl]amino]-5-

methyl-1-oxo-2-hexenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N,N.alpha.-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L141 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:501329 HCAPLUS
DN 127:109198
TI Inhibitors of interleukin-1.beta. converting enzyme
IN Bemis, Guy W.; Duffy, John P.; Fridman, Wolf Herman; Golec, Julian M. C.; Livingston, David J.; Mullican, Michael D.; Murcko, Mark A.; Zelle, Robert E.
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K005-00
ICS A61K038-55
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9722618	A1	19970626	WO 1996-US20370	19961220	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5843904	A	19981201	US 1995-575648	19951220	<--
	CA 2240489	AA	19970626	CA 1996-2240489	19961220	<--
	ZA 9610797	A	19970626	ZA 1996-10797	19961220	<--
	AU 9714658	A1	19970714	AU 1997-14658	19961220	<--
	AU 722936	B2	20000817			
	EP 876395	A1	19981111	EP 1996-945237	19961220	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO					
	CN 1207743	A	19990210	CN 1996-199733	19961220	<--
	BR 9612191	A	19990713	BR 1996-12191	19961220	<--
	NZ 326555	A	20000327	NZ 1996-326555	19961220	<--
	JP 2000503635	T2	20000328	JP 1997-523008	19961220	<--
	US 6162790	A	20001219	US 1998-24537	19980217	<--
	NO 9802774	A	19980819	NO 1998-2774	19980616	<--

PRAI US 1995-575648 A 19951220 <--
WO 1996-US20370 W 19961220
OS MARPAT 127:109198
AB Compds. R5(NHCHR4CO)nNR3CH2CONHCH[CH(OR2)(OR1)](CH2)mCO2R [R = H, (un)substituted alkyl; R1, R2 = R6, COR6, CONHR6 (R6 = aryl, alkyl, aralkyl, etc.); R1 and R2 may form a satd. cyclic group; or corresponding anhydrides for the case of R = R1 = H; R3 = arylmethyl, non-arom. cyclic group; R4 = (un)substituted alkyl; R5 = COR6, CO2H or ester or amide derivs., SO2R6, COCOR6, R6, H; m = 1, 2; n = 0-2] were prepd. as inhibitors of interleukin-1.beta. converting enzyme (ICE). Thus, (S)-Bz-L-Val-N(Bzl)CH2CONHCH(CH2CO2CO2H)CHO was prepd. via peptide coupling in soln. and found to have an ICE inhibition const. (Ki) of 69 nM.
ST peptide prepn inhibitor interleukin 1b
IT Intestine, disease
(Crohn's; inhibitors of interleukin-1.beta. converting enzyme)
IT Respiratory distress syndrome
(adult; inhibitors of interleukin-1.beta. converting enzyme)
IT Stomach, disease
(autoimmune gastritis; inhibitors of interleukin-1.beta. converting enzyme)
IT Anemia (disease)
(autoimmune hemolytic anemia; inhibitors of interleukin-1.beta. converting enzyme)
IT Thyroid gland, disease
Thyroid gland, disease
(autoimmune thyroiditis; inhibitors of interleukin-1.beta. converting enzyme)
IT Transplant and Transplantation
(graft-vs.-host reaction; inhibitors of interleukin-1.beta. converting enzyme)
IT Intestine, disease
(inflammatory; inhibitors of interleukin-1.beta. converting enzyme)
IT **Alzheimer's disease**
Asthma
Graves' disease
Multiple myeloma
Myasthenia gravis
Osteoarthritis
Osteoporosis
Parkinson's disease
Psoriasis
Rheumatoid arthritis
(inhibitors of interleukin-1.beta. converting enzyme)
IT Interleukin 1.beta.
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors of interleukin-1.beta. converting enzyme)
IT Peptides, preparation
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors of interleukin-1.beta. converting enzyme)
IT Diabetes mellitus
(insulin-dependent)
IT **Brain, disease**
Heart, disease
(**ischemia**; inhibitors of interleukin-1.beta. converting enzyme)
IT Leukemia
(myelogenous; inhibitors of interleukin-1.beta. converting enzyme)
IT Pancreas, disease
(pancreatitis; inhibitors of interleukin-1.beta. converting enzyme)
IT Connective tissue

(scleroderma; inhibitors of interleukin-1.beta. converting enzyme)
IT Lupus erythematosus
(systemic; inhibitors of interleukin-1.beta. converting enzyme)
IT Platelet (blood)
(thrombocytopenia; inhibitors of interleukin-1.beta. converting enzyme)
IT Hepatitis
(viral, chronic active; inhibitors of interleukin-1.beta. converting enzyme)
IT 192582-92-6P 192582-96-0P 192583-04-3P 192583-05-4P 192583-09-8P
192583-10-1P 192583-11-2P 192583-13-4P 192583-15-6P 192583-17-8P
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192583-30-5P 192583-31-6P 192583-32-7P 192583-33-8P 192583-34-9P
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192583-39-4P 192583-40-7P 192583-41-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors of interleukin-1.beta. converting enzyme)
IT 74-11-3, 4-Chlorobenzoic acid 94-53-1, Piperonylic acid 100-52-7, Benzaldehyde, reactions 118-41-2, 3,4,5-Trimethoxybenzoic acid, reactions 121-92-6, 3-Nitrobenzoic acid 367-27-1, 2,4-Difluorophenol 500-22-1, 3-Pyridinecarboxaldehyde 609-89-2 623-33-6, Glycine ethyl ester hydrochloride 1996-41-4 2338-18-3, 2-Aminoindan hydrochloride 5292-43-3, tert-Butyl bromoacetate 13734-41-3 21507-95-9, 2-Aminoisoindoline 68858-20-8 143305-33-3 175211-71-9 192583-42-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(inhibitors of interleukin-1.beta. converting enzyme)
IT 364-31-8P 6344-42-9P 58348-98-4P 83402-63-5P 192582-88-0P
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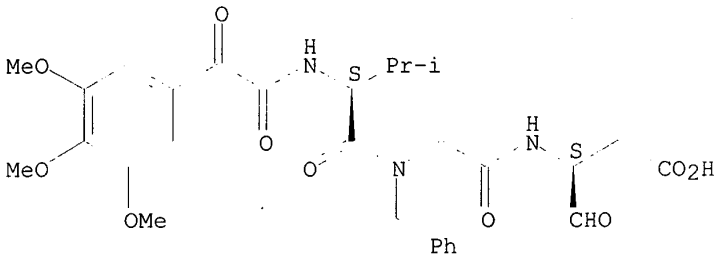
192583-14-5P 192583-16-7P 192583-18-9P 192583-19-0P 192583-20-3P
192583-22-5P 192583-24-7P 192583-26-9P 192583-43-0DP, resin-bound
192583-44-1DP, resin-bound 192583-45-2DP, resin-bound 192583-46-3DP, resin-bound 192583-47-4DP, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(inhibitors of interleukin-1.beta. converting enzyme)
IT 192582-93-7P 192582-95-9P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibitors of interleukin-1.beta. converting enzyme)
IT 192583-28-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(inhibitors of interleukin-1.beta. converting enzyme)
IT **192583-36-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors of interleukin-1.beta. converting enzyme)
RN 192583-36-1 HCAPLUS
CN Glycinamide, N-[oxo(3,4,5-trimethoxyphenyl)acetyl]-L-valyl-N-[(1S)-2-carboxy-1-formylethyl]-N2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:397372 HCAPLUS
DN 127:13470
TI **Neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders
IN **Steiner, Joseph P.; Hamilton, Gregory S.**
PA **Guilford Pharmaceuticals Inc., USA**
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-445
ICS A61K031-40
CC 1-11 (Pharmacology)
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9716190	A1	19970509	WO 1996-US13624	19960826	<--
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	US 2002013344	A1	20020131	US 1995-551026	19951031	<--
	US 5801197	A	19980901	US 1996-645149	19960513	<--
	AU 9668573	A1	19970522	AU 1996-68573	19960826	<--
	AU 713302	B2	19991125			
	EP 859614	A1	19980826	EP 1996-929014	19960826	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI					
	JP 11514643	T2	19991214	JP 1996-517308	19960826	<--
	ZA 9608982	A	19980907	ZA 1996-8982	19961025	
	NO 9801903	A	19980630	NO 1998-1903	19980427	<--
PRAI	US 1995-551026	A	19951031	<--		
	US 1996-645149	A	19960513			
	WO 1996-US13624	W	19960826			

OS MARPAT 127:13470
AB A method is disclosed of using specially formulated **neurotrophic** pipecolic acid derivs. (Markush included) having an affinity for **FKBP**-type **immunophilins** as inhibitors of **rotamase** enzyme activity to stimulate or promote **neuronal** growth or **regeneration**. The compds. of the invention may be used in treatment of **neurodegenerative** disorders , e.g. **Alzheimer**'s disease, **Parkinson**'s disease, and other **neuropathies**.
ST pipecolic acid deriv **immunophilin rotamase** inhibitor; **neurodegeneration Alzheimer**'s **Parkinson**'s

pipecolic acid deriv; **neurotrophic factor** pipecolic acid deriv **neurodegeneration; FKBP immunophilin rotamase** pipecolic acid deriv

IT Immunosuppressants
((non)immunosuppressant **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506-binding protein**); pipecolic acid derivs. **neurotrophic** action in relation to inhibition of **rotamase** activity of **FKBP**-type **immunophilins**)

IT **Immunophilins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP**-type; pipecolic acid derivs. **neurotrophic** action in relation to inhibition of **rotamase** activity of **FKBP**-type **immunophilins**)

IT **Neurotrophic factors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**brain-derived; neurotrophic** pipecolic acid **derivs.** as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **Nerve**
(**degeneration**, prevention; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **Nervous system**
(**degeneration; neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT Heregulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glial growth factor; neurotrophic** pipecolic acid **derivs.** as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **Brain, disease**
Spinal cord
(**injury; neurotrophic** pipecolic acid **derivs** . as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **Nerve**
(**neuron, regeneration** promoters; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **Nerve, disease**
(**neuropathy, peripheral; neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **Alzheimer's disease**
Parkinson's disease
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **Ciliary neurotrophic factor**
Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **Brain, disease**
(**stroke; neurotrophic** pipecolic acid **derivs** . as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT 535-75-1D, Pipecolic acid, derivs. **141083-86-5**
141084-02-8 141084-12-0 141084-13-1
141084-14-2 141084-34-6 141084-35-7
141084-39-1 141084-41-5 141084-42-6
141084-63-1 141097-91-8 145912-40-9
145913-15-1 145913-16-2 186834-74-2
186834-75-3 188614-85-9 188614-86-0
188614-94-0 188614-99-5 188615-02-3
188615-05-6 188615-14-7 190444-03-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders)

IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders)

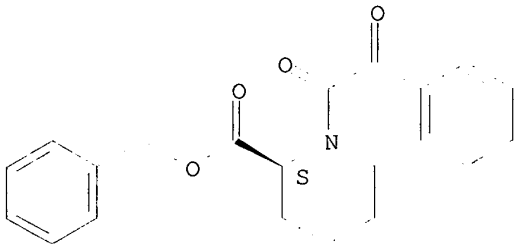
IT **130939-66-1, Neurotropin 3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic factors**)

IT **141083-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders)

RN 141083-86-5 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:307496 HCAPLUS
DN 126:272378
TI Methods and compositions for stimulating **neurite** growth using compds. with affinity for **FKBP12** in combination with **neurotrophic factors**
IN Armistead, David M.
PA Vertex Pharmaceuticals Incorporated, USA
SO S. African, 54 pp.
CODEN: SFXXAB
DT Patent
LA English
IC ICM C07D
ICS A61K
CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	ZA 9604852	A	19960729	ZA 1996-4852	19960607	<--
	US 6037370	A	20000314	US 1995-486004	19950608	<--
	CA 2222430	AA	19961227	CA 1996-2222430	19960606	<--
	WO 9641609	A2	19961227	WO 1996-US10123	19960606	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	AU 9661119	A1	19970109	AU 1996-61119	19960606	<--
	EP 831812	A2	19980401	EP 1996-918469	19960606	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	CN 1202104	A	19981216	CN 1996-195690	19960606	<--
	BR 9609333	A	19991013	BR 1996-9333	19960606	<--
	NZ 310339	A	20000327	NZ 1996-310339	19960606	<--
	NZ 501709	A	20001027	NZ 1996-501709	19960606	<--
	JP 2002502355	T2	20020122	JP 1997-503275	19960606	<--
	IL 122346	A1	20020523	IL 1996-122346	19960606	<--
	US 6124328	A	20000926	US 1997-795956	19970228	<--
	US 6326387	B1	20011204	US 2000-616539	20000714	<--
PRAI	US 1995-486004	A	19950608	<--		
	NZ 1996-310339	A1	19960606			
	WO 1996-US10123	W	19960606			
	US 1997-795956	A3	19970228			

OS MARPAT 126:272378
AB A pharmaceutically acceptable compn. is disclosed which comprises (a) a **neurotropic** amt. of a compd. with affinity for **FK-506-binding protein FKBP12** e.g.

having the formula BAC(:O)CH(K)N(J)C(:O)C(:E)D [A = O, NH, N(C1-4 alkyl); B = H, C1-6 (branched) alkyl, C2-6 (branched) alkenyl, C5-7 cycloalkyl, etc.; D = U; E = O, CHU (if D = H, then E = CH-U; if E = O, then D is not H); U = H, O-(C1-4)-straight or branched alkyl, O-(C2-4)-straight or branched alkenyl, C1-6 (branched) alkyl, C2-6 (branched) alkenyl, (substituted) C5-7 cycloalkyl, (substituted) C5-7 cycloalkenyl, etc.; J = H, C1-2 alkyl; K = C1-4 (branched) alkyl, benzyl, cyclohexylmethyl, or J and K taken together form 5-7 membered heterocyclic ring which may contain O, S, SO, SO2; and the stereochem. at carbon to which K is bonded = R or S] and pharmaceutically acceptable derivs. thereof; (b) a **neurotrophic factor**; and (c) a pharmaceutically carrier. The **neurotrophic factor** may be e.g. **nerve growth factor**. The methodol. of the invention can be used to promote repair of **neuronal** damage caused by disease or phys. trauma.

ST **FKBP12** compd neutrotrophic factor **neurite** growth; **nerve** damage **FKBP12** compd neutrotrophic factor

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP-12 (FK 506-binding protein, 12,000-mol.-wt.**); compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Nervous system**
(amyotrophic lateral sclerosis; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Neurotrophic factors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**brain-derived**; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Alzheimer's disease**
Axon
Drug delivery systems
Nervous system agents
Parkinson's disease
(compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Ciliary neurotrophic factor**
Neurotrophic factors
Platelet-derived **growth factors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Nerve**
(**degeneration**; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Nerve, disease**
(**facial, injury**, crush; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Neurotrophic factors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glial**-derived; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Spinal cord**
(injury; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Nerve, disease**
(**motor**; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Nerve**
(**neuron**; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Nerve, disease**
(**sciatic, injury**, crush; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT Ischemia
(**stroke**-assocd.; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **Brain, disease**
(**stroke**; compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT **9061-61-4, Nerve growth factor**
61912-98-9, IGF 61912-98-9D, IGF, truncated derivs. **94726-50-8**
106096-92-8, Acidic fibroblast **growth factor**
106096-93-9, Basic fibroblast **growth factor**
108415-25-4 130939-66-1, Neurotrophin 3
141083-86-5 141083-87-6 141083-88-7 141083-89-8
141083-90-1 141083-91-2 141083-92-3
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143375-33-1, **Neurotrophin** 4 145912-40-9
145913-35-5 148499-03-0, **Neurotrophin** 5
159997-62-3 159997-63-4 159997-65-6
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188615-54-5 188615-55-6 188615-56-7
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188615-60-3 188615-61-4 188615-62-5
188615-63-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

IT 188615-64-7 188615-65-8 188615-66-9
188615-67-0 188615-68-1 188615-69-2
188615-70-5 188615-71-6 188615-72-7
188618-35-1 189008-26-2 189008-27-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite**

growth)

IT **9061-61-4, Nerve growth factor**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with affinity for **FKBP12** in combination with **neurotrophic factors** for stimulating **neurite** growth)

RN 9061-61-4 HCAPLUS
CN Nerve growth factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L141 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:165074 HCAPLUS
DN 126:152815
TI **Rotamase** inhibitors for treatment of **neurological** diseases
IN **Steiner, Joseph P.**; Synder, Solomon; **Hamilton, Gregory S.**
PA **Guilford Pharmaceuticals, Inc., USA**; Johns Hopkins University School of Medicine
SO Jpn. Kokai Tokkyo Koho, 41 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K031-445
ICS A61K031-435; A61K031-50; A61K031-71; A61K038-00; C07D211-60; C07D491-04
CC 1-11 (Pharmacology)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08333256	A2	19961217	JP 1996-132866	19960430 <--
	JP 3060373	B2	20000710		
	US 5798355	A	19980825	US 1995-474072	19950607 <--
	CN 1187127	A	19980708	CN 1996-194555	19960605 <--
	LT 4516	B	19990625	LT 1998-2	19980106 <--
PRAI	US 1995-474072	A	19950607 <--		

AB **Rotamase** or **peptidyl-prolyl isomerase** inhibitors e.g. **neurotrophic** pipecolinic acid derivs. (including FK506, Way 124666, Rapamycin, SLB 506, etc.) with **FKBP**-type **immunophilin** affinity are claimed for stimulating **nerve** growth and **regeneration** after **nerve** injury in treatment of **neurol.** diseases e.g. **Alzheimer's** disease, **parkinsonism**, muscle atrophy, etc. The effects of these inhibitors were comparable to that of **nerve growth factor.**

ST **rotamase** inhibitor pipecolinate **neurol** disease

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506-binding protein**); **rotamase** inhibitors for treatment of **neurol.** diseases)

IT Muscle, disease
(atrophy; **rotamase** inhibitors for treatment of **neurol.** diseases)

IT **Nervous system**
(**disease**; **rotamase** inhibitors for treatment of **neurol. diseases**)

IT **Alzheimer's disease**
Parkinson's disease

(**rotamase** inhibitors for treatment of **neurol.** diseases)

IT **Immunophilins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**rotamase** inhibitors for treatment of **neurol.** diseases)

IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; **rotamase** inhibitors for treatment of **neurol.** diseases)

IT 535-75-1D, Pipecolinic acid, derivs. 53123-88-9, Rapamycin
104987-11-3, FK506 **141084-63-1 145021-24-5**
145021-25-6 145021-36-9 145021-37-0 145021-38-1 145021-39-2
145021-41-6 145021-43-8 145021-46-1 145021-47-2 145021-65-4
145021-66-5 145021-67-6 145021-68-7 145037-51-0 **147438-29-7**
147438-30-0 **147438-31-1 148493-28-1** 149438-31-3
152754-34-2 152754-35-3 152754-36-4
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155255-24-6 155255-27-9 155255-28-0
155255-29-1 155255-30-4 155255-31-5
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155668-50-1 155668-51-2 155668-52-3
155668-53-4 155668-54-5 155668-55-6
155668-56-7 155668-57-8 155668-58-9
155668-59-0 155668-61-4 155668-63-6 155668-64-7 156038-45-8
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186959-70-6 186959-77-3 186960-01-0 **186960-09-8**
186974-30-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rotamase** inhibitors for treatment of **neurol.** diseases)

IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; **rotamase** inhibitors for treatment of **neurol.** diseases)

RN 95076-93-0 HCAPLUS
CN Isomerase, peptidylprolyl cis-trans- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L141 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:155088 HCAPLUS
DN 126:153650
TI Regulation of biological processes using rapamycin and **FK506-binding proteins** fusion proteins
IN Clackson, Timothy; Holt, Dennis A.; Gilman, Michael Z.
PA Ariad Gene Therapeutics, Inc., USA; Clackson, Timothy; Holt, Dennis A.; Gilman, Michael Z.
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-10

ICS C12N009-90; C12N015-12; C12N015-10; C12N015-31; C12N015-62; C12N015-63; C12N015-85; C12N015-86; C07K014-395; C07K014-47; C07K014-715; C12Q001-68; A01K067-027

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 6

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9641865	A1	19961227	WO 1996-US9948	19960607	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	CA 2219080	AA	19961227	CA 1996-2219080	19960607	<--
	AU 9662706	A1	19970109	AU 1996-62706	19960607	<--
	AU 714904	B2	20000113			
	EP 833894	A1	19980408	EP 1996-921491	19960607	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2002514893	T2	20020521	JP 1997-503244	19960607	<--
	US 6187757	B1	20010213	US 1998-12097	19980122	<--
	US 2002107189	A1	20020808	US 2001-781804	20010212	<--
PRAI	US 1995-481941	A	19950607	<--		
	US 1996-598776	A	19960209			
	US 1996-15502P	P	19960209			
	WO 1996-US9948	W	19960607			
	US 1997-791044	A2	19970128			
	US 1998-12097	A3	19980122			

OS MARPAT 126:153650

AB A method using rapamycin to regulate gene expression or other processes in animal systems is described. The method uses fusion proteins of an **FK506-binding protein** (**FKBP**) and the DNA-binding domain of a transcription factor, and of a protein capable of binding to **FKBP**:rapamycin complexes such as FRAP, Tor1, Tor2 with an activation domain. Rapamycin and the **FKBP** and **FKBP**:rapamycin-**binding protein** form a bridge that brings the DNA-binding and activation domains together to form an active transcription factor in the presence of rapamycin. The method can be generally applied to any process regulated by proteins with a similar domain structure.

ST rapamycin gene expression regulation; FRAP fusion protein gene expression regulation; **FKBP12** fusion protein gene expression regulation; **FKBP** fusion protein gene expression regulation

IT **Proteins, specific or class**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**FKBP** (**FK 506-binding protein**), fusion products; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT **Proteins, specific or class**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**FKBP-12** (**FK 506-binding protein, 12,000-mol.-wt.**), analogs, fusion products; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Proteins, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(FRAP (**FKBP**-rapamycin-assocd. protein), fusion products; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(GAL4, fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(IRES (internal ribosomal entry site) element, in bicistronic expression vectors; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(NF-.kappa.B (nuclear factor .kappa.B), p65 subunit fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(VP16, fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT RNA formation factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(ZFHD1, fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Gene
(expression, regulation by rapamycin of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Chimeric gene
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for transcription factor fusion products with **FKBP12** and FRAP; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Fas antigen
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(fusion products, in rapamycin regulation of gene expression;

regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene TOR1, fusion products; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene TOR2, fusion products; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene lexA, fusion products with rapamycin-**binding proteins**, regulation of DNA binding by; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Promoter (genetic element)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interleukin 2, rapamycin regulation of gene expression from; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Peptide library
(of fusion proteins contg. modified **FKBP** domains; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(p19BL87G6FKBP, chimeric gene for LexA-**FKBP** fusion protein, rapamycin regulation of DNA binding in relation to; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(p19BL87G6FRB, chimeric gene for LexA-FRB fusion protein, rapamycin regulation of DNA binding in relation to; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Tumor necrosis factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p55, fusion products with rapamycin-**binding proteins**; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-1FRAPe-ZFHD1, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-1FRAPe-p65(361-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-1FRAPe-p65(450-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-1FRB-VP16, VP16-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-1FRB-p65(361-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-1FRB-p65(361-550)-IRES-ZFD1-3FKBP, chimeric genes for FRAP-NF-.kappa.B p65 subunit and ZFD1-**FKBP** fusion proteins on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-1FRB-p65(450-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-2FRAPe-ZFHD1, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-2FRB-VP16, VP16-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-2FRB-p65(450-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-3FRAPe-p65(361-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-3FRAPe-p65(450-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-3FRB, gene for FLAG-labeled FRB on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPb-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPc-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPd-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPe-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPa-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-GAL-2FRB, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)
IT Plasmid vectors
(pCGNN-GAL-3FRB, GAL4-FRAP fusion protein gene on; regulation of biol.

processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-4FRB, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPb, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPc, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPd, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPe, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPf, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPg, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPh, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPi, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPa, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-1FRB, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-2FRAPe, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-2FRB, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-3FRAPe, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-4FRAPe, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding** **proteins** fusion proteins)

IT Plasmid vectors

(pCGNN-ZFHD1-FRAPb, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-FRAPe, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-FRAPa, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-p65(361-550)-1FRAPe, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-p65(361-550)-3FRAPe, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-p65(450-550)-1FRAPe, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNN-p65(450-550)-3FRAPe, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNNZFHD1-**FKBPx1**, ZFHD1-**FKBP12** fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pCGNNZFHD1-**FKBPx3**, ZFHD1-**FKBP12** fusion protein gene on; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pZHWTx12-CMV-SEAP, secreted alk. phosphatase reporter gene on, rapamycin regulation of expression of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pZHWTx12-CMV-hGH, human growth hormone reporter gene on, rapamycin regulation of expression of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Plasmid vectors
(pZHWTx12-IL2-SEAP, secreted alk. phosphatase reporter gene on, rapamycin regulation of expression from IL2 promoter of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Myristoylation
(peptide target for, incorporation into **FKBPs** of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT **Nerve growth factor receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(p75, fusion products with **FKBP** and FRAP, in rapamycin regulation of apoptosis; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Interleukin 2

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rapamycin regulation of expression from promoter of gene for;
regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT Apoptosis
Cell differentiation
Cell proliferation
Signal transduction, biological
Transcription, genetic
(regulation by rapamycin of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT CD3 (antigen)
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(.zeta.-chain, fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 80449-02-1, Protein tyrosine kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation by rapamycin of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 186847-32-5 186847-34-7 186847-36-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 162926-18-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(biotinylation of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 104987-11-3, **FK506**
RL: RCT (Reactant); RACT (Reactant or reagent)
(conjugation with fluorescein of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 186845-13-6 186845-14-7
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence, chimeric genes contg.; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 186847-33-6 186847-35-8 186847-37-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 152406-15-0P 154074-71-2P 186757-74-4P 186757-77-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reactions of, in prepn. fluoresceinated **FK506**; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 186757-82-4P
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(prepn. of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 186757-79-9P 186757-80-2P 186757-81-3P

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(rapamycin analog, binding to FRAP of complexes with **FKBP**; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT **178446-27-0**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(rapamycin analog, regulation of apoptosis using; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT 53123-88-9D, Rapamycin, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

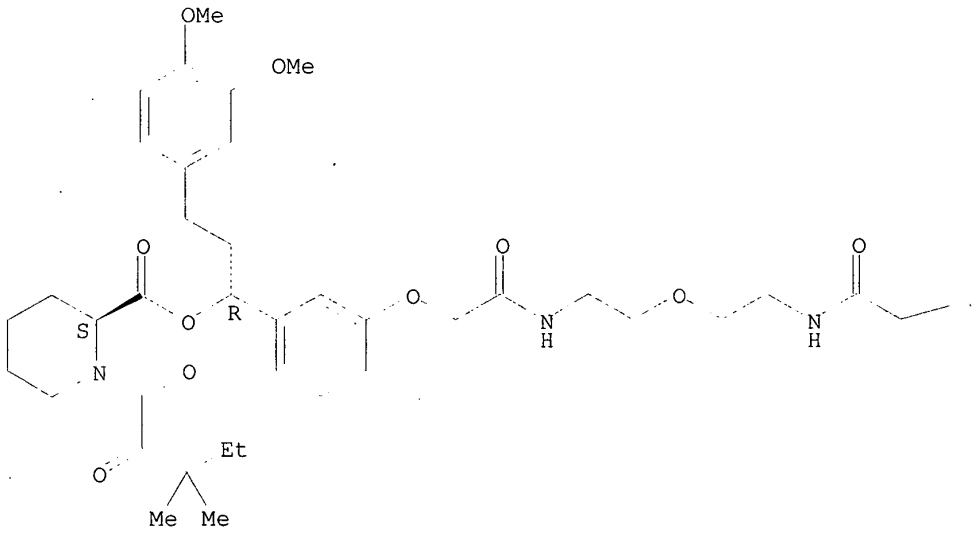
IT 161754-08-1P 161754-09-2P 186757-66-4P 186757-67-5P 186757-68-6P 186757-69-7P 186757-70-0P 186757-71-1P 186757-72-2P 186757-73-3P 186794-75-2P 186794-97-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

IT **178446-27-0**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(rapamycin analog, regulation of apoptosis using; regulation of biol. processes using rapamycin and **FK506-binding proteins** fusion proteins)

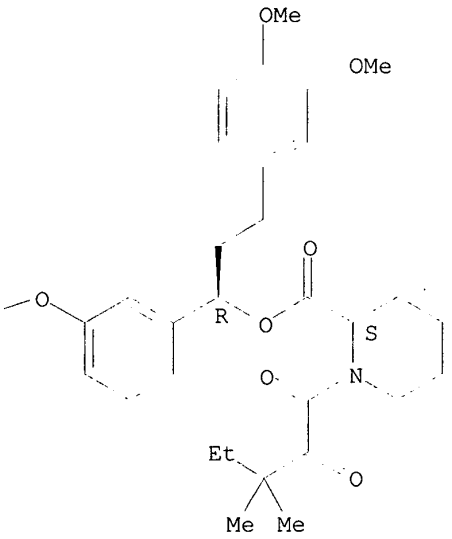
RN 178446-27-0 HCAPLUS
CN 2-Piperidinecarboxylic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)-, oxybis[2,1-ethanediylimino(2-oxo-2,1-ethanediyl)oxy-3,1-phenylene[(1R)-3-(3,4-dimethoxyphenyl)propylidene]] ester, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L141 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:151523 HCAPLUS
DN 126:152817
TI Pipecolic acid derivatives as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.
IN **Steiner, Joseph P.**; Snyder, Solomon; **Hamilton, Gregory S.**
PA **Guilford Pharmaceuticals Inc., USA**; Johns Hopkins University School of Medicine
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-495
ICS A61K031-50; A61K031-44; A61K031-445
CC 1-11 (Pharmacology)
Section cross-reference(s): 7
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9640140	A1	19961219	WO 1996-US9561	19960605	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	US 5798355	A	19980825	US 1995-474072	19950607	<--
	US 5696135	A	19971209	US 1996-653905	19960528	<--
	AU 9661622	A1	19961230	AU 1996-61622	19960605	<--
	AU 710423	B2	19990923			
	GB 2305605	A1	19970416	GB 1996-24258	19960605	<--
	GB 2305605	B2	20000112			
	DE 19680255	T	19970605	DE 1996-19680255	19960605	<--
	EP 777478	A1	19970611	EP 1996-919227	19960605	<--
	EP 777478	B1	20011107			
	R: BE, FR, GR, IE, IT, MC, NL					

BR 9608485	A	19990706	BR 1996-8485	19960605	<--
NZ 310767	A	20001124	NZ 1996-310767	19960605	<--
FI 9604137	A	19970115	FI 1996-4137	19961015	<--
SE 9604097	A	19961208	SE 1996-4097	19961108	<--
DK 9601256	A	19961220	DK 1996-1256	19961108	<--
NO 9704290	A	19971204	NO 1997-4290	19970917	<--
PRAI US 1995-474072	A	19950607	<--		
US 1996-653905	A	19960528			
WO 1996-US9561	W	19960605			

AB **Neurotrophic** pipecolic acid **derivs.** having an affinity for **FKBP**-type **immunophilins** are useful as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, and in particular inhibitors of **peptidyl-prolyl isomerase** or **rotamase** enzyme activity, to stimulate or promote **neuronal** growth or **regeneration.** The compds, of the invention (e.g. Way-124,666; SLB-506) are useful for the treatment of **neurol.** disorders. The compds. may be used in conjunction with a **neurotrophic factor** (**neurotrophic growth factor, brain-derived growth factor, neurotropin-3,** etc.).

ST pipecolic acid deriv **rotamase** inhibitor; **nervous** system disorder pipecolic acid deriv; **nerve** growth **regeneration** pipecolic acid deriv

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506-binding protein**), **FKBP**-type **immunophilins**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT Biological transport
(**FKBP** transport in sciatic **nerve**)

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP-12** (**FK 506-binding protein, 12,000-mol.-wt.**); pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Immunophilins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP**-type; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nervous system**
(amyotrophic lateral sclerosis; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve**
(**degeneration**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nervous system**
(**disease**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Brain, disease**
Spinal cord
(**injury**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve**
(**myelinated**, myelination recovery; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Regeneration**, animal
(**nerve**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve, disease**
(**peripheral neuropathy**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve, disease**
(**peripheral, injury**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Alzheimer's disease**
Immunosuppressants
Nervous system agents
Parkinson's disease
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Neurotrophic factors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT GAP-43 (protein)
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve**
(**regeneration**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Ganglion**
(**spinal**; FK506 as **neurotrophic** for sensory ganglia)

IT **Brain, disease**
(**stroke, brain** damage-assocd.; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **130939-66-1, Neurotropin-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in combination with **neurotrophic factor** in treatment of **nervous** system disorders.)

IT **9061-61-4, Nerve growth factor**
53123-88-9, Rapamycin 59865-13-3, Cyclosporin A 104987-11-3, FK-506
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT 535-75-1D, Pipecolic acid, derivs. **141084-63-1**
145021-24-5 145021-25-6 145021-28-9 145021-36-9
145021-37-0 145021-38-1 145021-41-6 145021-43-8 145021-47-2
145021-65-4 145021-66-5 145021-67-6 145021-68-7 145037-51-0
147438-30-0 **147438-31-1 148493-28-1** 149438-31-3,
Way-124466 **152754-34-2 152754-35-3 152754-36-4**

152754-37-5 152754-38-6 152754-40-0
152754-41-1 152754-42-2 152754-45-5 **153011-31-5,** SBL
506 **155255-24-6 155255-25-7 155255-27-9**
155255-28-0 155255-29-1 155255-30-4
155255-31-5 155255-32-6 155367-80-9
155399-01-2 155399-02-3 155399-09-0
155668-46-5 155668-47-6 155668-49-8
155668-50-1 155668-51-2 155668-52-3
155668-53-4, 2-Piperidinecarboxylic acid, 1-(1,2-dioxopropyl)-,
ethyl ester, (.+-.)- **155668-54-5 155668-55-6**
155668-56-7 155668-57-8 155668-58-9
155668-59-0 155668-60-3 155668-61-4 155668-63-6 155668-64-7
155668-86-3 155668-89-6 156038-45-8 157634-33-8
157634-34-9 157634-35-0 157757-22-7 **157757-23-8**
157757-24-9 **158631-86-8** 164913-78-4 164913-79-5
164913-80-8 165047-17-6 186834-56-0 186834-57-1 186834-58-2
186834-59-3 186834-60-6 186834-61-7 **186834-62-8**
186834-63-9 186834-64-0 186834-65-1
186834-66-2 186834-67-3 186834-68-4
186834-69-5 186834-70-8 186834-71-9
186834-72-0 186834-73-1 186834-74-2
186834-75-3 186834-76-4 186834-77-5
186834-78-6 186834-79-7 186834-80-0
186834-81-1 186834-82-2 186834-83-3
186834-84-4 186834-85-5 186834-86-6
186834-87-7 186834-88-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **130939-66-1, Neurotropin-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in combination with **neurotrophic factor** in treatment of **nervous** system disorders.)

RN 130939-66-1 HCAPLUS
CN Neurotrophin 3 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

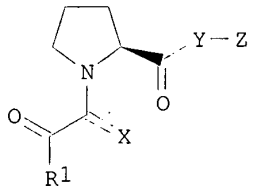
L141 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:127457 HCAPLUS
DN 126:144545
TI Preparation of **immunophilin**-binding glyoxalylproline esters as **rotamase** enzyme activity inhibitors
IN **Hamilton, Gregory S.; Steiner, Joseph P.**
PA **Guilford Pharmaceuticals Inc., USA**
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D207-16
ICS A61K031-40
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 15, 63

FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9640633	A1	19961219	WO 1996-US9701	19960605	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	US 5614547	A	19970325	US 1995-479436	19950607	<--
	US 5859031	A	19990112	US 1996-650461	19960521	<--
	AU 9661062	A1	19961230	AU 1996-61062	19960605	<--
	AU 703118	B2	19990318			
	GB 2305176	A1	19970402	GB 1996-24257	19960605	<--
	GB 2305176	B2	19991222			
	EP 769006	A1	19970423	EP 1996-918384	19960605	<--
	EP 769006	B1	20001108			
	R: BE, FR, GR, IE, IT, MC, NL					
	DE 19680256	T	19970619	DE 1996-19680256	19960605	<--
	BR 9608444	A	19990105	BR 1996-8444	19960605	<--
	JP 2000503626	T2	20000328	JP 1997-501958	19960605	<--
	AT 9609002	A	20010215	AT 1996-9002	19960605	<--
	AT 408187	B	20010925			
	EE 200000317	A	20010615	EE 2000-20000031719960605		<--
	RU 2186770	C2	20020810	RU 1997-111860	19960605	<--
	FI 9604328	A	19961230	FI 1996-4328	19961028	<--
	SE 9604098	A	19961208	SE 1996-4098	19961108	<--
	NO 9704213	A	19971204	NO 1997-4213	19970912	<--
PRAI	US 1995-479436	A	19950607	<--		
	US 1996-650461	A	19960521			
	WO 1996-US9701	W	19960605			

OS MARPAT 126:144545

GI



I

AB This invention relates to **neurotrophic** N-glyoxyl-prolyl esters I [R1 = straight or branched C1-9 alkyl or alkenyl optionally substituted with C3-8 cycloalkyl; C3 or C5 cycloalkyl, C5-7 cycloalkenyl, or Ar1 substituted with 0-3 halo, OH, NO2, CF3, C1-6 straight or branched alkyl or alkenyl, C1-4 alkoxy, C1-4 alkenyloxy, PhO, PhCH2O,or amino; Ar1 = naphthyl, 2- or 3-indolyl, furyl, 2-thiazolyl, thienyl, pyridyl, Ph; X = O, S, CH2, H2; Y = O, NR2; R2 = H, C1-6 alkyl; Z = C2-6 straight of branched alkyl or alkenyl substituted by one or more Ar1, C3-8 cycloalkyl, cycloalkyl connected by C1-6 straight or branched alkyl or alkenyl chain, CHR3COX2R4; R3 = straight or branched C1-8 alkyl optionally substituted with C3-8 cycloalkyl or Ar1; X2 = O, NR5; R5 = H, C1-6 straight or branched alkyl or alkenyl; R4 = Ph, CH2Ph, C1-5 straight or branched alkyl or alkenyl, C1-5 straight or branched alkyl or alkenyl substituted with Ph] or pharmaceutically acceptable salts or hydrates thereof, having an

affinity for **FKBP**-type **immunophilins**, their prepn. and use as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, and particularly inhibitors of **peptidyl-prolyl isomerase** or **rotamase** enzyme activity. Thus, coupling of H-L-Pro-OMe with MeO2CCOCl, followed by addn. of EtCMe2MgCl gave glyoxalylproline ester EtCMe2COCO-L-Pro-OMe (II). Sapon. of II followed by esterification with Ph(CH2)3OH gave a desired title compd., EtCMe2COCO-L-Pro-O(CH2)2Ph. (III). Prepd. inhibitors, including III, were tested for inhibition of **peptidyl-prolyl isomerase**, for **neurite** outgrowth in chick doral root ganglion, and in a MPTP model of **Parkinson**'s disease in mice.

ST **FKBP12 immunophilin** inhibitor glyoxalylproline ester prepn

IT **Proteins, specific or class**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP-12** (**FK 506-binding protein, 12,000-mol.-wt.**); prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **Antiparkinsonian agents**
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **Immunophilins**
Neurotrophic factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **186268-50-8P 186268-51-9P 186268-52-0P**
186268-53-1P 186268-54-2P 186268-56-4P
186268-57-5P 186268-58-6P 186268-63-3P
186268-64-4P 186268-65-5P 186268-66-6P
186268-67-7P 186268-68-8P 186452-05-1P
186452-06-2P 186452-07-3P 186452-08-4P
186452-09-5P 186452-10-8P 186452-11-9P
186452-12-0P 186452-13-1P 186452-14-2P
186452-15-3P 186452-16-4P 186452-17-5P
186452-18-6P 186452-19-7P 186452-20-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **186268-55-3 186268-59-7 186268-60-0**
186268-62-2 186268-69-9 186268-71-3
186268-72-4 186268-73-5 186268-74-6
186268-75-7 186268-76-8 186452-22-2
186452-23-3 186452-24-4 186452-25-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **95076-93-0, Peptidyl-prolyl isomerase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT 122-97-4, 3-Phenyl-1-propanol 2133-40-6, L-Proline methyl ester hydrochloride 5781-53-3, Methyl oxalyl chloride 28276-08-6, 1,1-Dimethylpropylmagnesium chloride
RL: RCT (Reactant); RACT (Reactant or reagent)

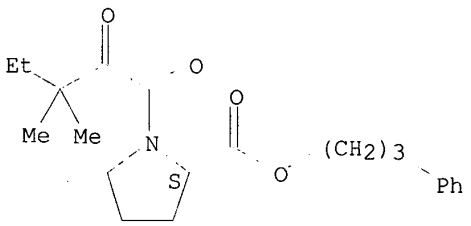
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **139419-63-9P 186268-77-9P** 186268-78-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **186268-50-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

RN 186268-50-8 HCAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxopentyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:113367 HCAPLUS
DN 126:122464
TI Novel cathepsin Y and methods and compositions for inhibition thereof
IN Tung, Jay S.; Sinha, Sukanto; Mcconlogue, Lisa; Tatsuno, Gwen; Anderson, John; Semko, Christopher M. F.; Chrysler, Susanna
PA Athena Neurosciences, Inc., USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K048-00
ICS C12Q001-68; C07H021-02; C07H021-04
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 7, 34
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9639194	A1	19961212	WO 1996-US6211	19960426	<--
	W: CA, JP					
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 5783434	A	19980721	US 1995-467607	19950606	<--
	US 5849711	A	19981215	US 1995-469362	19950606	<--
	CA 2221684	AA	19961212	CA 1996-2221684	19960426	<--
	EP 831920	A1	19980401	EP 1996-913917	19960426	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 11506923	T2	19990622	JP 1996-500507	19960426	<--
	US 5858982	A	19990112	US 1997-850392	19970502	<--
PRAI	US 1995-467607		19950606	<--		
	US 1995-469362		19950606	<--		
	WO 1996-US6211		19960426			

OS MARPAT 126:122464

AB Methods for inhibiting the secretion of .beta.-**amyloid** peptide (.beta.AP) from cells comprise administering to the cells certain compds. which inhibit the activity of an approx. 31 kD protease involved in .beta.AP secretion. The 31 kD protease has been designated Cathepsin Y. Screening methods for .beta.AP inhibitors rely on detg. the activity of test compds. in the presence of Cathepsin Y and a suitable peptide substrate. This invention is also directed to a nucleic acid sequence that encodes Cathepsin Y and the expression and isolation of Cathepsin Y.

ST cathepsin Y inhibitor **amyloid** secretion blocker

IT Animal cell line
(293; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Drug delivery systems
(capsules; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Drug delivery systems
(inhalants; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Drug delivery systems
(injections, i.v.; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Drug delivery systems
(injections; novel cathepsin Y and methods and compns. for inhibition thereof)

IT **Alzheimer's disease**
Molecular cloning
Protein sequences
Transformation, genetic
cDNA sequences
(novel cathepsin Y and methods and compns. for inhibition thereof)

IT mRNA
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(novel cathepsin Y and methods and compns. for inhibition thereof)

IT Hydrocarbon waxes, biological studies
Paraffin oils
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(novel cathepsin Y and methods and compns. for inhibition thereof)

IT Peptides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(oligopeptides; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Drug delivery systems
(oral; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Glycerides, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(satd. fatty-acid-contg.; novel cathepsin Y and methods and compns. for inhibition thereof)

IT **Brain, disease**
(**senile plaque**; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Drug delivery systems
(suppositories; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Drug delivery systems
(suspensions; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Drug delivery systems

(tablets; novel cathepsin Y and methods and compns. for inhibition thereof)

IT **Amyloid**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(.beta.-; novel cathepsin Y and methods and compns. for inhibition thereof)

IT Gene, animal
RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(.beta.-**amyloid**-encoding; novel cathepsin Y and methods and compns. for inhibition thereof)

IT 9004-08-4, Cathepsin
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(Y; novel cathepsin Y and methods and compns. for inhibition thereof)

IT 186209-14-3P, Cathepsin Y (human 293 cell)
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); CAT (Catalyst use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(amino acid sequence; novel cathepsin Y and methods and compns. for inhibition thereof)

IT 7631-86-9, Silicon dioxide, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(colloidal; novel cathepsin Y and methods and compns. for inhibition thereof)

IT 9004-34-6, Cellulose, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(microcryst.; novel cathepsin Y and methods and compns. for inhibition thereof)

IT 174962-85-7 174962-98-2 186030-20-6 186030-24-0 186030-28-4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(novel cathepsin Y and methods and compns. for inhibition thereof)

IT 174962-97-1 186030-21-7 186030-22-8 186030-23-9 186030-25-1 186030-26-2 186030-29-5
RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)
(novel cathepsin Y and methods and compns. for inhibition thereof)

IT 57-50-1, Sucrose, biological studies 63-42-3 532-32-1, Sodium benzoate 557-04-0, Magnesium stearate 9003-39-8, Polyvinylpyrrolidone 9005-25-8, Starch, biological studies 9063-38-1, Sodium carboxymethyl starch 11138-66-2, Xanthan gum
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(novel cathepsin Y and methods and compns. for inhibition thereof)

IT 59830-60-3P 65178-14-5P 88191-84-8P 121253-52-9P 123392-26-7P
133410-84-1P 144345-63-1P 145428-03-1P 148743-43-5P 161710-37-8P
163039-91-6P 167498-28-4P 168633-31-6P 186030-30-8P 186030-31-9P
186030-32-0P 186030-33-1P 186030-34-2P 186030-35-3P 186030-36-4P
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186030-54-6P 186030-55-7P 186030-56-8P **186030-57-9P**
186030-58-0P 186030-59-1P **186030-60-4P** 186030-61-5P
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186030-67-1P 186030-68-2P 186030-69-3P 186030-70-6P 186030-71-7P
186030-72-8P 186030-73-9P **186030-74-0P** 186030-75-1P

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186030-85-3P 186030-86-4P 186030-87-5P 186030-88-6P 186030-89-7P
186030-90-0P 186030-91-1P 186030-92-2P 186030-93-3P 186030-94-4P
186030-95-5P 186030-96-6P 186030-97-7P 186030-98-8P 186030-99-9P
186186-16-3P
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel cathepsin Y and methods and compns. for inhibition thereof)

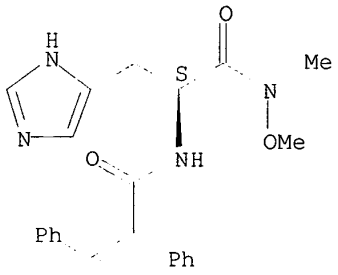
IT 60-24-2, .beta.-Mercaptoethanol 643-79-8, o-Phthalaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel cathepsin Y and methods and compns. for inhibition thereof)

IT 186209-15-4P
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(nucleotide sequence; novel cathepsin Y and methods and compns. for inhibition thereof)

IT **186030-57-9P**
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel cathepsin Y and methods and compns. for inhibition thereof)

RN 186030-57-9 HCAPLUS
CN 1H-Imidazole-4-propanamide, N-methoxy-N-methyl-.alpha.-[(1-oxo-2,3-diphenyl-2-propenyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



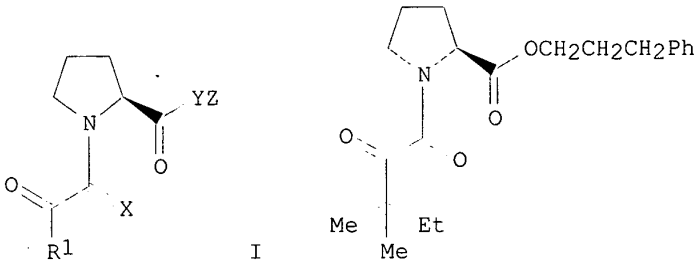
L141 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:113317 HCAPLUS
DN 126:118197
TI Preparation of proline derivatives as **rotamase** inhibitors
IN **Hamilton, Gregory S.**
PA **Guilford Pharmaceuticals,inc., USA**
SO Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07D207-16
ICS A61K031-40; A61K038-00; C07D407-04; C07D409-04; C07D417-04; C07K005-078; C12N009-99
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 27
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08333334	A2	19961217	JP 1995-246895	19950831 <--
	US 5614547	A	19970325	US 1995-479436	19950607 <--

	JP 2002371058	A2	20021226	JP 2002-113933	19950831	<--
	CN 1187188	A	19980708	CN 1996-194554	19960605	<--
	ZA 9608984	A	19980625	ZA 1996-8984	19961025	<--
	LT 4484	B	19990325	LT 1998-1	19980106	<--
PRAI	US 1995-479436	A	19950607	<--		
	JP 1995-246895	A3	19950831	<--		

OS MARPAT 126:118197

GI



AB The title compds. I [R1 = alkyl, etc.; Z = lipophilic group; X = O, S, etc.; Y = O, NH, etc.] are prepd. I are also **neurotropic** compds. with affinity for **immunophilins**. The title compd. II in vitro showed the Ki value of 42 nM in a test for **rotamase** inhibiting activity.

ST proline deriv prepn **rotamase** inhibitor **neurotropic**

IT Proteins, general, biological studies
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of proline derivs. with effect on **immunophilins**)

IT **186268-50-8P 186268-51-9P 186268-52-0P**
186268-53-1P 186268-54-2P 186268-55-3P
186268-56-4P 186268-57-5P 186268-58-6P
186268-59-7P 186268-60-0P 186268-61-1P
186268-62-2P 186268-63-3P 186268-64-4P
186268-65-5P 186268-66-6P 186268-67-7P
186268-68-8P 186268-69-9P 186268-70-2P
186268-71-3P 186268-72-4P 186268-73-5P
186268-74-6P 186268-75-7P 186268-76-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. as **rotamase** inhibitors)

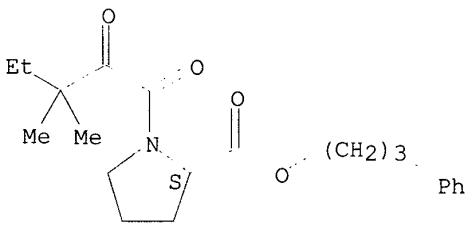
IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of proline derivs. as **rotamase** inhibitors)

IT 86-81-7, 3,4,5-Trimethoxybenzaldehyde 100-52-7, Benzaldehyde, reactions 103-63-9, 2-(Bromoethyl)benzene 122-97-4, 3-Phenyl-1-propanol 2133-40-6, L-Proline methyl ester hydrochloride 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 3182-93-2, L-Phenylalanine ethyl ester hydrochloride 5781-53-3, Methyl oxalyl chloride 28276-08-6, 1,1-Dimethylpropylmagnesium chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of proline derivs. as **rotamase** inhibitors)

IT 1083-30-3P 4407-36-7P 14097-24-6P 20329-96-8P 30273-62-2P 40918-96-5P 53560-26-2P 58095-76-4P 68889-69-0P 82475-75-0P **139419-63-9P** 148775-22-8P **186268-77-9P** 186268-78-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of proline derivs. as **rotamase** inhibitors)

IT **186268-50-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. as **rotamase** inhibitors)
RN 186268-50-8 HCAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxopentyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1996:748345 HCAPLUS
DN 126:19332
TI Preparation of peptides as modulators of **amyloid** aggregation
IN Findeis, Mark A.; Benjamin, Howard; Garnick, Marc B.; Gefter, Malcolm L.; Hundal, Arvind; Kasman, Laura; Musso, Gary; Signer, Ethan R.; Wakefield, James; et al.
PA Pharmaceutical Peptides Incorporated, USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-47
ICS A61K038-17
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9628471	A1	19960919	WO 1996-US3492	19960314 <--
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5817626	A	19981006	US 1995-404831	19950314 <--
	US 5854215	A	19981229	US 1995-475579	19950607 <--
	AU 9652524	A1	19961002	AU 1996-52524	19960314 <--
	EP 815134	A1	19980107	EP 1996-908805	19960314 <--
	EP 815134	B1	20020605		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11514333	T2	19991207	JP 1996-527816	19960314 <--
	AT 218583	E	20020615	AT 1996-908805	19960314 <--
PRAI	US 1995-404831	A	19950314 <--		
	US 1995-475579	A	19950607 <--		
	US 1995-548998	A	19951027 <--		
	WO 1996-US3492	W	19960314		

AB Compds. that modulate the aggregation of **amyloidogenic** proteins or peptides are disclosed. The modulators of the invention can promote **amyloid** aggregation or, more preferably, can inhibit natural **amyloid** aggregation. In a preferred embodiment, the compds. modulate the aggregation of natural .beta. **amyloid** peptides

(.beta.-AP). In a preferred embodiment, the .beta. **amyloid** modulator compds. of the invention are comprised of an A.beta. aggregation core domain and a modifying group coupled thereto such that the compd. alters the aggregation or inhibits the **neurotoxicity** of natural .beta. **amyloid** peptides when contacted with the peptides. Furthermore, the modulators are capable of altering natural .beta.-AP aggregation when the natural .beta.-APs are in a molar excess amt. relative to the modulators. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for **amyloidogenic** diseases using the compds. of the invention, are also disclosed. These peptide compds. are bound to natural .beta.-**amyloid** peptides to facilitate diagnosis of a .beta.-**amyloidogenic** disease, in particular **Alzheimer**'s disease, and are useful for treating a disorder assocd. with **amyloidosis** including, e.g. familial **amyloid** polyneuropathy or cardiomyopathy, isolated cardiac **amyloid**, systemic senile **amyloidosis**, scrapie, bovine spongiform encephalopathy, and Creutzfeldt-Jakob disease. Thus, N-biotinyl-DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV-OH (N-biotinyl-.beta.-AP1-40), prepd. by the solid phase synthesis using a N.alpha.-Fmoc-based protection strategy and Fmoc-Val-Wang resin, at 1% markedly inhibited aggregation of the natural .beta.-**amyloid** peptide (.beta.-AP1-40).

ST peptide prepn modulator **amyloid** aggregation; diagnosis **amyloidogenic** disease **Alzheimer** disease; **amyloidosis** assocd disorder; familial **amyloid** polyneuropathy cardiomyopathy treatment peptide; isolated cardiac **amyloid** treatment peptide; systemic senile **amyloidosis** treatment peptide; scrapie treatment peptide; bovine spongiform encephalopathy treatment peptide; Creutzfeldt Jakob disease treatment peptide

IT **Brain, disease**
Prion diseases
(**Creutzfeldt-Jakob**; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Deafness
Urticaria
(Muckle-Wells syndrome in familial Mediterranean Fever and familial **amyloid** nephropathy; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Diagnosis
(agents, for **Alzheimer**'s disease; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Heart, disease
Heart, disease
(**amyloidosis**, isolated; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Nervous system**
(**disease, Gerstmann-Straussler syndrome**; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Amyloidosis**
Amyloidosis
(familial Mediterranean fever, with Muckle-Wells syndrome; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Fever and Hyperthermia
Fever and Hyperthermia
(familial Mediterranean, with Muckle-Wells syndrome; prepn. of peptides as modulators of **amyloid** aggregation for treating

amyloidosis-assocd. disorders)

IT Kidney, disease
(familial **amyloid** nephropathy with Muckle-Wells syndrome and fibrinogen-assocd. hereditary renal **amyloidosis**; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Heart, disease
(familial **amyloidotic** cardiomyopathy; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Amyloidosis**
(familial **amyloidotic** polyneuropathy, type IV; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Amyloidosis**
(familial **amyloidotic** polyneuropathy; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Dialysis
(hemodialysis, **amyloidosis** assocd. with long term hemodialysis; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Brain, disease**
(**hemorrhage**, hereditary cerebral **hemorrhage** with **amyloidosis** of Iceland type; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis** -assocd. disorders)

IT **Amyloidosis**
(hereditary, lysozyme-assocd.; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Pancreatic islet of Langerhans
(insulinoma; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Carcinoma
(medullary, **amyloidosis** assocd. with thyroid medullary carcinoma; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Macroglobulins
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(metabolic disorders, macroglobulinemia, myeloma or macroglobulinemia-assocd. **amyloidosis**; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Multiple myeloma
(myeloma or macroglobulinemia-assocd. **amyloidosis**; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Diabetes mellitus
(non-insulin-dependent; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Nerve, disease**
(**polyneuropathy**, familial **amyloid**; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Amyloid**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PREP (Preparation)
(prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT Sjogren's syndrome
(primary localized cutaneous nodular **amyloidosis**-assocd.; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Amyloidosis**
(primary; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Brain, disease**
Prion diseases
(scrapie; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Amyloidosis**
(secondary; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Amyloidosis**
(senile, systemic; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Brain, disease**
(**spongiform encephalopathy**; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT **Alzheimer's disease**
(treatment and diagnosis; prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT 123529-23-7P 153247-40-6P 156858-22-9P 182912-78-3P 183745-74-6P
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184051-31-8P 184051-32-9P 184051-33-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

IT 58-85-5, Biotin 64-19-7, Acetic acid, reactions 67-43-6 81-25-4, Cholic acid 40248-63-3, (-)-Menthoxyacetic acid 68858-20-8D, Wang resin-bound 72088-94-9 131438-79-4 183745-73-5 183745-81-5 183745-82-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of peptides as modulators of **amyloid** aggregation for

treating **amyloidosis**-assocd. disorders)

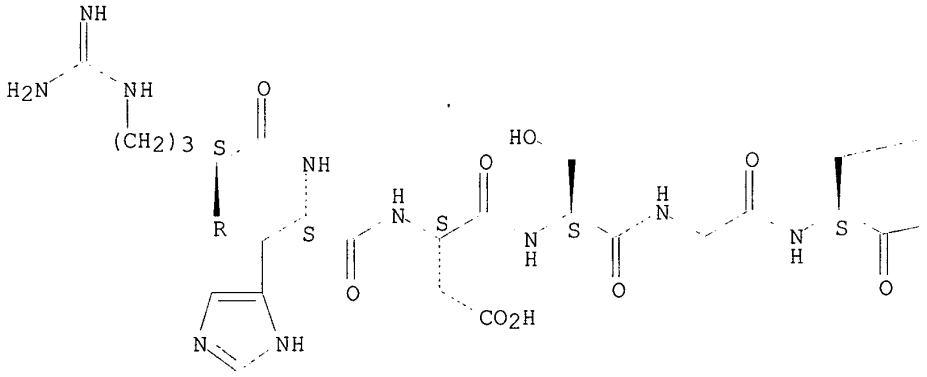
IT **183745-94-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides as modulators of **amyloid** aggregation for treating **amyloidosis**-assocd. disorders)

RN 183745-94-0 HCAPLUS

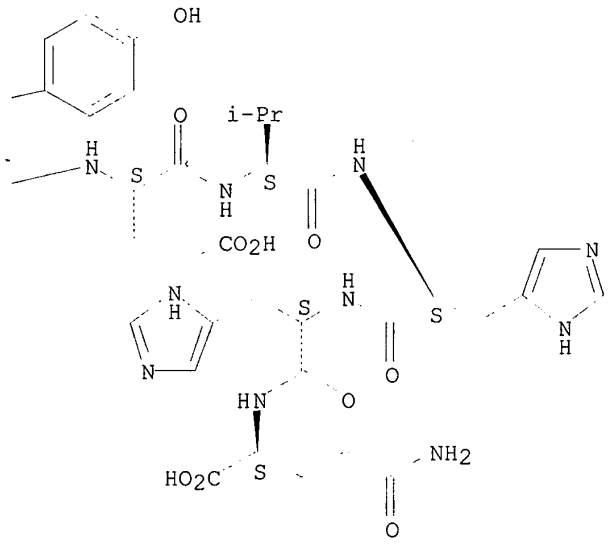
CN L-Glutamine, N-(N-acetylneuraminoyl)-L-.alpha.-aspartyl-L-alanyl-L-.alpha.-glutamyl-L-phenylalanyl-L-arginyl-L-histidyl-L-.alpha.-aspartyl-L-serylglycyl-L-tyrosyl-L-.alpha.-glutamyl-L-valyl-L-histidyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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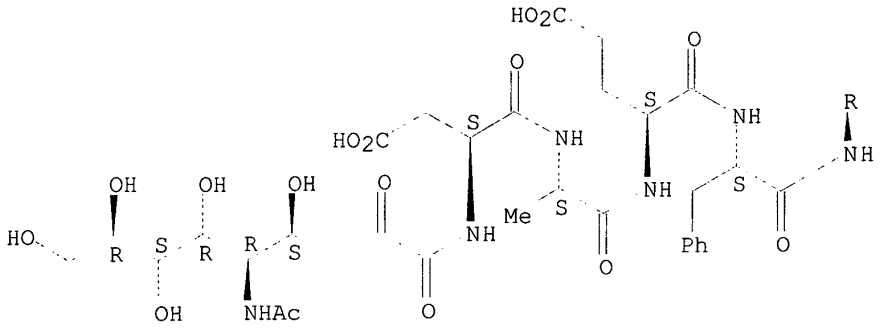

L141 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1996:593837 HCAPLUS
DN 125:248490
TI Butyryl-tyrosinyl spermine and analogs thereof inhibiting binding of etiological agent to glutamate receptor, and methods of preparing and using same
IN Nakanishi, Koji; Huang, Danwen; Choi, Seok-Ki; Kalivretenos, Aristotle; Goodnow, Robert
PA Trustees of Columbia University in the City of New York, USA
SO PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C211-00
ICS C07C235-00; C07C229-00; C07D209-04; A61K031-135; A61K031-16; A61K031-20; A61K031-405; A61K031-40
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 5
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9622962	A1	19960801	WO 1996-US1128	19960123 <--
	W: AU, CA, JP, MX, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6001824	A	19991214	US 1995-376924	19950123 <--
	AU 9651684	A1	19960814	AU 1996-51684	19960129 <--
PRAI	US 1995-376924		19950123 <--		
	US 1988-153151		19880208 <--		
	US 1991-701223		19910516 <--		
	US 1994-275336		19940714 <--		
	WO 1996-US1128		19960123		

OS MARPAT 125:248490
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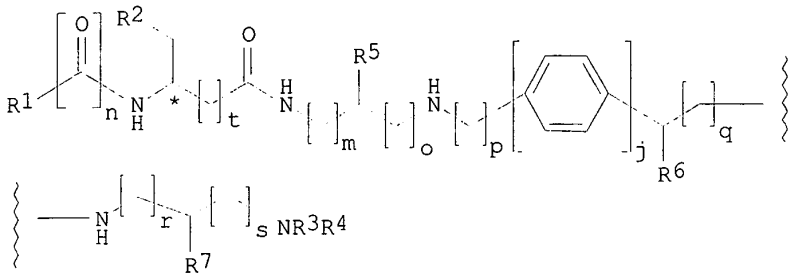

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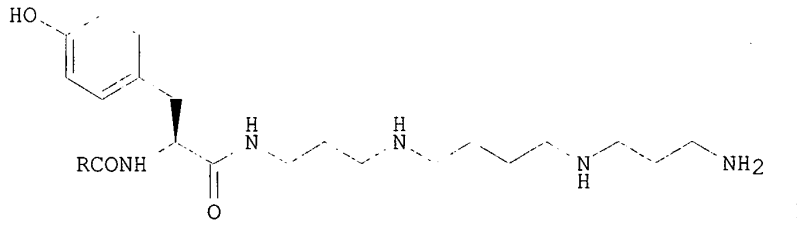

II

AB Compds. having structure [I; R1 = satd. or unsatd. linear or branched chain alkyl, or cholestanyl; R2 = 2-, 3-, 4-, or 5-indolyl, 4-hydroxyphenyl, 4-(arylalkyloxy)phenyl, 3,4-dihalophenyl, 4-hydroxy-3,5-dihalophenyl, 4-azidophenyl, 4-halophenyl; R3 = H, linear or branched chain alkyl or alkenyl group, or Ph, 2-, 3-, or 4-azidophenyl, alkenylacyl, 3-amino-3-butylpropyl, N-[N-[N-(4-azidobenzoyl)aminopropyl]aminopropyl], cis- or trans-cinnamyl, 2-amino-2-[(4'-azidophenyl)acetyl], (trifluoromethyl)-aminoacetyl, D- or L-arginyl group bonded through the .alpha.-carbonyl moiety thereof; R4 = H, linear or branched chain alkyl; R5, R6, R7 = H, linear or branched chain alkyl, aryl, arylalkyl; n, j, t = 0, 1; m, o, p, q, r, s = 0, 1, 2; r + s and m + o = 2; when j = 0, p + q = 2; if j = 1, p = 1, q = 0, and R6 = H; * denotes a D or L configuration], which inhibit binding of an etiol. agent to a quisqualate glutamate receptor, in particular N-methyl-D-aspartate receptor, are prepd. Another aspect of the invention concerns a method of treating a subject afflicted by a disorder assocd. with binding of an etiol. agent to a glutamate receptor. These compds. are useful for treating a **neurodegenerative** disease (Huntington's disease, **Parkinson**'s disease, or **Alzheimer**'s disease), movement disorder such as epilepsy, or a **stroke**-related disorder assocd. with excessive binding of glutamate receptors. An insecticidal compn. comprising I is also claimed. Thus, p-nitrophenyl N-butyryl-O-benzyl-L-tyrosinate was condensed with spermine in MeOH to give N-butyryl-O-benzyl-L-tyrosine spermine amide (II) and bis(N-butyryl-O-benzyl-L-tyrosine) spermine amide. II was hydrogenolyzed in the presence of 5% Pd-C in MeOH to give philanthotoxin-343 (III; R = n-Pr). The latter compd. and III (R = n-nonyl) showed IC50 of 1.3 .times. 10-5 and 1.4 .times. 10-6 M, resp., for antagonizing the **neurally**-evoked twitch contraction of the locust Schistocerca gregaria metathoracic extensor tibiae muscle.

ST butyryltyrosinylspermine prepn glutamate receptor antagonist; tyrosinylspermine butyryl prepn glutamate receptor antagonist; philanthotoxin analog quisqualate glutamate receptor antagonist; methylaspartate receptor antagonist; **neurodegenerative** disease treatment butyryltyrosinylspermine; Huntington disease treatment butyryltyrosinylspermine; **Parkinson** disease treatment butyryltyrosinylspermine; **Alzheimer** disease treatment butyryltyrosinylspermine; epilepsy treatment butyryltyrosinylspermine;

stroke treatment butyryltyrosinylspermine

IT Insecticides
(prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor)

IT Anticonvulsants and Antiepileptics
Parkinsonism
(prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor for disease therapy)

IT **Mental disorder**
(**Alzheimer**'s disease, prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor for disease therapy)

IT **Nervous system**
(**disease**, Huntington's chorea, prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor for **disease** therapy)

IT **Neurotransmitter** antagonists
(glutamatergic, N-methyl-D-aspartate receptor; prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor for disease therapy)

IT **Brain, disease**
(**stroke**, prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor for disease therapy)

IT 105029-41-2P 115976-91-5P 115976-92-6P 115976-93-7P 122306-15-4P
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181783-18-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor for disease therapy)

IT 71-44-3, Spermine 100-02-7, p-Nitrophenol, reactions 107-13-1, 2-Propenenitrile, reactions 109-65-9, 1-Bromobutane 110-60-1, 1,4-Diaminobutane 112-13-0, Decanoyl chloride 141-75-3, Butyryl chloride 501-53-1, Benzyl chloroformate 623-27-8, 1,4-Benzenedicarboxaldehyde 1956-08-7, p-Nitrophenyl heptanoate 2130-96-3 2592-19-0 3556-56-7 3655-05-8 16652-64-5 24424-99-5, Di-tert-butyl dicarbonate 40120-91-0 75178-96-0 132160-73-7 181524-71-0
RL: RCT (Reactant); RACT (Reactant or reagent)

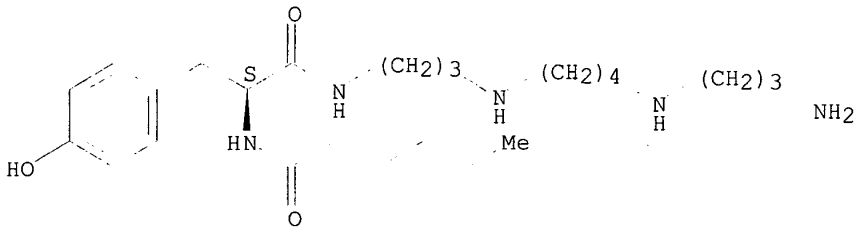
(prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor for disease therapy)

IT 4748-73-6P 13512-59-9P 15160-31-3P 42918-71-8P 57177-83-0P
68076-39-1P 68076-41-5P 125376-00-3P 125376-01-4P 125376-03-6P
130203-13-3P 130203-15-5P 130203-27-9P 130203-28-0P 130203-29-1P
130203-30-4P 130203-33-7P 130203-34-8P 130203-35-9P 130203-36-0P
130203-37-1P 130203-38-2P 130203-42-8P 142978-60-7P 175085-80-0P
175085-84-4P 181524-41-4P 181524-44-7P 181524-45-8P 181524-47-0P
181524-54-9P 181524-58-3P 181524-61-8P 181524-64-1P 181524-65-2P
181524-66-3P 181524-67-4P 181524-68-5P 181524-69-6P 181524-70-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor for disease therapy)

IT **130306-78-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-butyryltyrosinylspermine and analogs thereof as antagonists of glutamate receptor for disease therapy)

RN 130306-78-4 HCAPLUS
CN Benzenepropanamide, N-[3-[[4-[(3-aminopropyl)amino]butyl]amino]propyl]-4-hydroxy-.alpha.-[(1-oxo-2,4-hexadienyl)amino]-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L141 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:890017 HCAPLUS
DN 124:30401
TI Preparation of tryptophan esters and amides as tachykinin receptor antagonists
IN Dorn, Conrad P.; Maccoss, Malcolm; Mills, Sander G.; Shah, Shrenik K.
PA Merck and Co., Inc., USA
SO Brit. UK Pat. Appl., 58 pp.
CODEN: BAXXDU
DT Patent
LA English
IC ICM C07D209-14
ICS A61K031-405; A61K031-44; C07D401-12
ICI C07D401-12, C07D209-14, C07D213-56
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2282807	A1	19950419	GB 1994-20262	19941007 <--
PRAI US 1993-138515		19931015 <--		

OS MARPAT 124:30401
AB RCH2CH(NR2COR1)COZCHR4R5 [I; R = 3-indolyl; R1 = (un)substituted alkyl;

R2,R4 = H, alkyl; R5 = (un)substituted Ph; Z = O or NR8; R8 = H or Me] were prepd. as tachykinin receptor antagonists (no data). Thus, L-tryptophen benzyl ester was N-acylated with Ph2CHCH2CO2H and the sapond. product amidated with MeNHCH2Ph to give (S)-Ph2CH2CONHCH(CH2R)CONMeCH2Ph (R = 3-indolyl).

ST tryptophan ester prepn tachykinin receptor antagonist

IT Analgesics
(prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT Bronchodilators
(antiasthmatics, prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT **Nerve, disease**
(**neuralgia**, treatment; prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT **Nerve, disease**
(**neuropathy**, treatment; prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT **Nerve, disease**
(**peripheral, motor, neuropathy**, treatment; prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT Kinin receptors
Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinin NK1, antagonists; prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT 169673-09-0P 169673-31-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT 169673-02-3P 169673-03-4P 169673-04-5P 169673-05-6P 169673-10-3P
169673-11-4P 169673-12-5P 169673-13-6P 169673-14-7P 169673-15-8P
169673-16-9P 169673-17-0P 169673-18-1P 169673-19-2P 169673-20-5P
169673-21-6P **169673-22-7P** 169673-23-8P 169673-24-9P
169673-25-0P 169673-26-1P 169673-27-2P 169673-28-3P 169673-29-4P
169673-30-7P 169673-32-9P 169673-33-0P 169673-34-1P 169673-35-2P
169673-36-3P 169673-37-4P 169673-38-5P 169673-39-6P 169673-40-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT 103-67-3, N-Methylbenzylamine 368-63-8, .alpha.-Methyl-3,5-bis(trifluoromethyl)benzyl alcohol 401-95-6, 3,5-Bis(trifluoromethyl)benzaldehyde 606-83-7, 3,3-Diphenylpropionic acid 2050-92-2, Dipentylamine 2491-06-7, N,N-Dimethylglycine hydrochloride 13139-14-5, N.alpha.-Boc-L-tryptophan 17093-74-2, N-AcetylL-threonine 22809-37-6, 6-Bromohexanoyl chloride 32247-96-4, 3,5-Bis(trifluoromethyl)benzyl bromide 32707-89-4, 3,5-Bis(trifluoromethyl)benzyl alcohol 35858-81-2, L-Tryptophan benzyl ester hydrochloride 169673-43-2 169673-44-3, L-Tryptophan N-benzyl-N-methyl amide
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT 159820-24-3P 169673-06-7P 169673-07-8P 169673-08-9P 169673-41-0P
169673-42-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

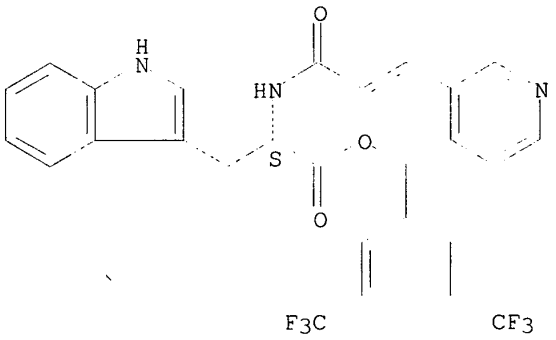
(Reactant or reagent)
(prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

IT **169673-22-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tryptophan esters and amides as tachykinin receptor antagonists)

RN 169673-22-7 HCAPLUS

CN L-Tryptophan, N-[1-oxo-3-(3-pyridinyl)-2-propenyl]-, [3,5-bis(trifluoromethyl)phenyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L141 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2003 ACS

AN 1995:861201 HCAPLUS

DN 123:256765

TI Preparation of pyrroloquinoxalinediones as excitatory amino acid antagonists

IN Lubisch, Wilfried; Behl, Berthold; Hofmann, Hans Peter

PA BASF A.-G., Germany

SO Ger. Offen., 30 pp.
CODEN: GWXXBX

DT Patent

LA German

IC ICM C07D403-10
ICS C07D401-14; A61K031-495

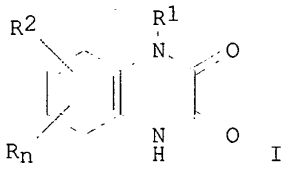
ICI C07D403-10, C07D241-44; C07D207-335; C07D401-14, C07D241-44; C07D213-40

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4340045	A1	19950601	DE 1993-4340045	19931124 <--
ZA 9409283	A	19960523	ZA 1994-9283	19941123 <--
CA 2208240	AA	19960627	CA 1994-2208240	19941221 <--
WO 9619476	A1	19960627	WO 1994-EP3839	19941221 <--
W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SI, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9513115	A1	19960710	AU 1995-13115	19941221 <--
EP 799224	A1	19971008	EP 1995-904415	19941221 <--
EP 799224	B1	20020417		
R: CH, DE, ES, FR, GB, IT, LI				
JP 10509131	T2	19980908	JP 1994-510491	19941221 <--
ES 2174919	T3	20021116	ES 1995-904415	19941221 <--

US 5849743 A 19981215 US 1997-860017 19970620 <--
PRAI DE 1993-4340045 A 19931124 <--
EP 1995-904415 A 19941221 <--
WO 1994-EP3839 W 19941221 <--
OS MARPAT 123:256765
GI



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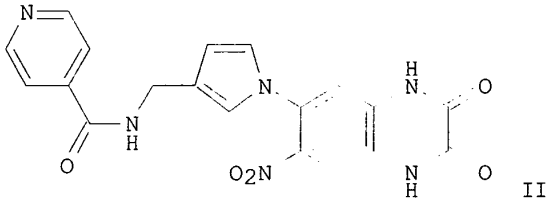


II

AB Title compds. [I; R = alkyl, halo, alkoxy, NO2, etc.; R1 = H, (un)substituted (cyclo)aliph. group; R2 = Z(CH2)mR6; R6 = piperidino, piperazino, pyrrolo, substituted HNCONH2, etc.; Z = 1-pyrrolylene; m = 1-4; n = 0-2] were prepd. Thus, 6-aminoquinoxaline-2,3(1H,4H)-dione was converted in 3 steps to 6-amino-7-nitroquinoxaline-2,3(1H,4H)-dione which was cyclocondensed with N-(2,5-dimethoxytetrahydrofuran-3-ylmethyl)isonicotinamide to give title compd. II.HOAc which had KI of <10.mu.M against binding of AMPA at rat **brain** membrane prepn.

ST pyrroloquinoxalinedione prepn excitatory amino acid antagonist; **nervous** system agent pyrroloquinoxalinedione prepn

IT Anticonvulsants and Antiepileptics
Antidepressants
Anxiolytics
(prepn. of pyrroloquinoxalinediones as excitatory amino acid antagonists)

IT **Nervous system**
(**disease, degeneration,** treatment; prepn. of pyrroloquinoxalinediones as excitatory amino acid antagonists)

IT Amino acid receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(excitatory, antagonists; prepn. of pyrroloquinoxalinediones as excitatory amino acid antagonists)

IT Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(excitatory amino acid, antagonists; prepn. of pyrroloquinoxalinediones as excitatory amino acid antagonists)

IT 169117-08-2P 169117-09-3P 169117-12-8P 169117-15-1P 169117-22-0P 169117-24-2P 169117-26-4P 169117-28-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of pyrroloquinoxalinediones as excitatory amino acid antagonists)

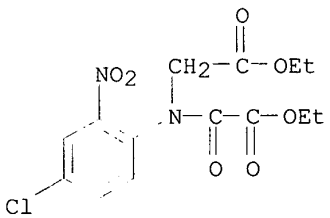
IT 169117-03-7P 169117-04-8P 169117-06-0P 169117-07-1P 169117-10-6P
169117-11-7P 169117-13-9P 169117-14-0P 169117-16-2P 169117-17-3P
169117-18-4P 169117-19-5P 169117-20-8P 169117-21-9P 169117-23-1P
169117-25-3P 169117-27-5P 169117-29-7P 169117-30-0P 169117-31-1P
169117-32-2P 169117-33-3P 169117-34-4P 169117-35-5P 169117-36-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrroloquinoxalinediones as excitatory amino acid antagonists)

IT 55-22-1, Isonicotinic acid, reactions 56-40-6, Glycine, reactions
89-61-2, 2,5-Dichloronitrobenzene 91-21-4, 1,2,3,4-Tetrahydroisoquinoline 92-54-6, N-Phenylpiperazine 93-04-9, 2-Methoxynaphthalene 103-71-9, Phenylisocyanate, reactions 108-91-8, Cyclohexylamine, reactions 504-24-5, 4-Aminopyridine 771-99-3, 4-Phenylpiperidine 841-77-0, 4-Benzhydrylpiperazine 2759-28-6, N-Benzylpiperazine 3173-56-6, Benzylisocyanate 6973-93-9, 6-Aminoquinoxaline-2,3(1H,4H)-dione 10338-69-9, 4-Phenyl-1,2,5,6-tetrahydropyridine 28356-58-3, 4-Pyridineacetic acid 50634-05-4, 2,5-Dimethoxytetrahydrofuran-3-carboxaldehyde 63921-23-3, 4-Amino-1-phenylpiperidine 65057-97-8 66893-77-4, 3-Aminomethyl-2,5-dimethoxytetrahydrofuran 118876-68-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyrroloquinoxalinediones as excitatory amino acid antagonists)

IT 4900-66-7P, 2-Methoxy-1-nitronaphthalene 59827-87-1P 66367-04-2P
87815-75-6P 139677-70-6P 154017-59-1P 154017-60-4P 169117-37-7P
169117-38-8P 169117-39-9P 169117-40-2P 169117-41-3P 169117-42-4P
169117-43-5P 169117-44-6P 169117-45-7P 169117-46-8P 169117-47-9P
169117-48-0P 169117-49-1P 169117-50-4P 169117-51-5P 169117-52-6P
169117-53-7P 169117-54-8P 169117-55-9P 169117-56-0P
169117-57-1P 169117-58-2P 169117-59-3P 169117-60-6P
169117-61-7P 169117-62-8P 169117-63-9P 169117-64-0P 169117-65-1P
169117-66-2P 169117-67-3P 169117-68-4P 169117-69-5P 169117-70-8P
169117-71-9P, 2-Amino-4-chloro-N-cyclohexylaniline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pyrroloquinoxalinediones as excitatory amino acid antagonists)

IT **169117-57-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pyrroloquinoxalinediones as excitatory amino acid antagonists)

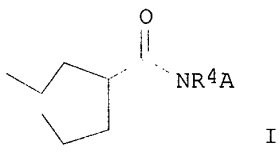
RN 169117-57-1 HCAPLUS
CN Glycine, N-(4-chloro-2-nitrophenyl)-N-(ethoxyoxoacetyl)-, ethyl ester (9CI) (CA INDEX NAME)



L141 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:787154 HCAPLUS
DN 123:199402
TI Preparation of amino acid amides containing derivatives of valproic acid as anticonvulsants
IN Bialer, Meir; Hadad, Salim; Herzig, Jacob; Sterling, Jeff; Lerner, David; Shirvan, Mitchell
PA Yissum Research Development Co., Israel; Teva Pharmaceutical Industrie, Ltd.
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C237-12
ICS C07C237-22; C07C233-01; A61K031-16; A61K031-275
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9501956	A1	19950119	WO 1994-US7498	19940706 <--
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5585358	A	19961217	US 1993-88074	19930706 <--
	CA 2143636	AA	19950119	CA 1994-2143636	19940706 <--
	AU 9473968	A1	19950206	AU 1994-73968	19940706 <--
	AU 673766	B2	19961121		
	ZA 9404884	A	19950220	ZA 1994-4884	19940706 <--
	EP 659174	A1	19950628	EP 1994-923915	19940706 <--
	EP 659174	B1	19990210		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1111907	A	19951115	CN 1994-190471	19940706 <--
	JP 08504831	T2	19960528	JP 1994-504097	19940706 <--
	HU 73771	A2	19960930	HU 1995-503	19940706 <--
	RO 113461	B1	19980730	RO 1995-475	19940706 <--
	AT 176664	E	19990215	AT 1994-923915	19940706 <--
	ES 2131207	T3	19990716	ES 1994-923915	19940706 <--
	RU 2140904	C1	19991110	RU 1995-108243	19940706 <--
	CZ 288328	B6	20010516	CZ 1995-853	19940706 <--
	SK 282456	B6	20020205	SK 1995-395	19940706 <--
	NO 9500849	A	19950426	NO 1995-849	19950303 <--
PRAI	US 1993-88074	A	19930706 <--		
	WO 1994-US7498	W	19940706 <--		

OS MARPAT 123:199402
GI



I

AB Title compds. I (A = NCCHR5, R3R2NCO(CH2)nCHR1 wherein R1-5 = H, C1-6 alkyl, aralkyl, n = 0-3), are prepd. I are also effective for treatment of other **neurol**. disorders. Valproyl chloride in CH2Cl2 was added to glycinamide-HCl to give N-(2-propylpentanoyl)glycinamide.

Anticonvulsant and **neurolog.** activities were demonstrated. I are claimed as pharmaceutical compns., affective illness, **neurodegenerative** disease, **neurotoxic** injury, etc.

ST amino acid amide prepn anticonvulsant; **neurol** disorder treatment amino acid amide

IT Anticonvulsants and Antiepileptics
(prepn. of amino acid amides contg. derivs. of valproic acid as anticonvulsants)

IT **Nervous system**
(**disease**, prepn. of amino acid amides contg. derivs. of valproic acid for treatment of)

IT 92262-58-3P 92262-61-8P 165406-57-5P 167629-60-9P 167629-61-0P
167629-64-3P 167629-65-4P 167629-66-5P 167629-67-6P
167629-69-8P 167629-70-1P 167629-71-2P 167629-72-3P
167629-73-4P 167629-74-5P 167629-76-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid amides contg. derivs. of valproic acid as anticonvulsants)

IT 109-73-9, Butylamine, reactions 1668-10-6, Glycinamide hydrochloride 2491-20-5, Alanine methyl ester hydrochloride 2936-08-5, Valproyl chloride 5680-79-5, Glycine methyl ester hydrochloride 6011-14-9, Aminoacetonitrile hydrochloride 10466-60-1, DL-Leucinamide hydrochloride 13515-97-4, DL-Alanine methyl ester hydrochloride 21969-70-0, Phenylglycinamide 22356-89-4 33786-48-0 52605-49-9, Sarcosine ethyl ester hydrochloride 165406-58-6 **167629-77-8** 167629-78-9
167629-79-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of amino acid amides contg. derivs. of valproic acid as anticonvulsants)

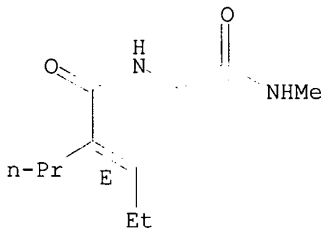
IT 167629-62-1P 167629-63-2P **167629-68-7P** 167629-75-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid amides contg. derivs. of valproic acid as anticonvulsants)

IT **167629-69-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid amides contg. derivs. of valproic acid as anticonvulsants)

RN 167629-69-8 HCAPLUS

CN 2-Pentenamide, N-[2-(methylamino)-2-oxoethyl]-2-propyl-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L141 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2003 ACS

AN 1995:731521 HCAPLUS

DN 123:144653

TI Preparation of peptide .alpha.-ketoamides as calpain inhibitors.
IN Harbeson, Scott L.; Straub, Julie Ann
PA Alkermes, Inc., USA
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K005-02
ICS C07K007-02; C07K005-06; C07K005-08; A61K037-64
CC 34-3 (Amino Acids, Peptides, and Proteins)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9500535	A1	19950105	WO 1994-US6497	19940609 <--
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5541290	A	19960730	US 1993-82274	19930624 <--
	AU 9472452	A1	19950117	AU 1994-72452	19940609 <--
PRAI	US 1993-82274		19930624 <--		
	WO 1994-US6497		19940609 <--		

OS MARPAT 123:144653
AB M(A1)xA2NHCHR1COCONHR2SO2R3 (sic), M(A1)xA2NHCHR1COCONHR5R6, etc.; [M = H, H2NCO, H2NCS, H2NSO2, R7CS, R7NHCS, R7CO, R7SO2, R7O2C, etc.; R7 = 1-adamantyl, (substituted) alkyl, alkyl, Ph, naphthyl, phenylalkyl, phenoxyalkyl, etc.; A1 = D-, L-, or nonchiral amino acid, e.g., Ala, Val, Leu, Ile, Met, Tyr, Asn, Gln, .beta.-Ala, Sar, Orn, O-ethylserine, pipecolinic acid, cyclohexylalanine, pyridylalanine, p-nitrophenylalanine, .alpha.-aminoheptanoic acid, citrulline, 2-azetidinecarboxylic acid, trifluoroleucine, etc.; x = 0-3; A2 = D- or L-amino acid capable of imparting calpain specificity; R1 = alkyl, cycloalkyl, fluoroalkyl; R2 = alkyl, cycloalkyl, phenylalkyl, (substituted) phenylalkyl, phenylcycloalkyl; R3 = R2, OH, OR2, NH2, NHR2; NR2R2; R5, R6 = H, alkyl, cycloalkyl, (substituted) phenylalkyl, phenylcycloalkyl, morpholinoalkyl, piperidinoalkyl, etc.], were prepd. Thus, Z-Leu-Abu-CONHEt (Abu = L-.alpha.-aminobutyric acid) (soln. phase prepn. given) inhibited calpain I with Ki = 77 nM.
ST peptide ketoamide prepn calpain inhibitor; **neurodegeneration** treatment peptide ketoamide
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide .alpha.-ketoamides as calpain inhibitors)
IT **Nerve, disease**
(**degeneration**, treatment; prepn. of peptide .alpha.-ketoamides as calpain inhibitors)
IT 144231-76-5P 144248-93-1P 153370-98-0P 153371-07-4P 153371-08-5P 160801-88-7P 160801-89-8P **160801-90-1P** 160801-91-2P 160801-92-3P 160868-23-5P 160868-27-9P 160868-28-0P 161021-87-0P **166195-97-7P 166195-98-8P 166195-99-9P 166196-00-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide .alpha.-ketoamides as calpain inhibitors)
IT 78990-62-2, Calpain
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of peptide .alpha.-ketoamides as calpain inhibitors)
IT 61-90-5, Leucine, reactions 79-44-7, Dimethylcarbamoyl chloride

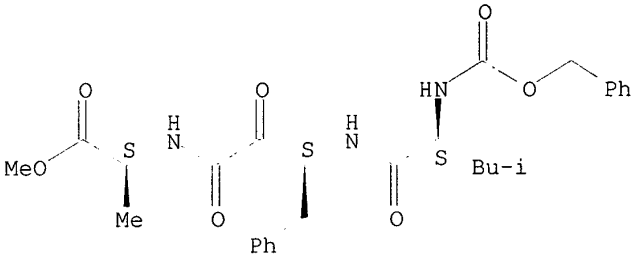
2018-66-8 3397-35-1 13139-15-6 13734-34-4 15159-40-7, 4-Morpholinecarbonyl chloride 17585-69-2 18942-49-9 34306-42-8 51482-39-4 54303-30-9, 2-(Ethylthio)ethylamine hydrochloride 62084-21-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of peptide .alpha.-ketoamides as calpain inhibitors)

IT 62000-68-4P 72155-45-4P 82848-28-0P 87694-53-9P 123206-29-1P 129739-09-9P 153371-25-6P 160801-72-9P 160801-73-0P 160801-74-1P 160868-33-7P 160868-34-8P 166196-01-6P 166196-02-7P 166196-03-8P 166196-04-9P 166196-05-0P 166196-06-1P 166196-07-2P 166196-08-3P 166196-09-4P 166196-10-7P 166375-04-8P 166375-05-9P 166375-06-0P 166375-07-1P 166375-08-2P 166375-09-3P 166375-10-6P 166375-11-7P 166375-12-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptide .alpha.-ketoamides as calpain inhibitors)

IT **160801-90-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide .alpha.-ketoamides as calpain inhibitors)

RN 160801-90-1 HCAPLUS
CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-, methyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:380330 HCAPLUS
DN 122:151382
TI preparation of alkylthiofatty acid derivatives and their uses in treating liver, kidney, pancreas, and **brain** diseases
IN Kurobe, Hiroshi; Nunosawa, Tetsuji; Sanada, Kunio; Sugawara, Tomoaki; Matsutani, Yoshihide; Moriguchi, Yukie; Endo, Takeshi
PA Fuji Chem Ind Co Ltd, Japan
SO Jpn. Kokai Tokkyo Koho, 57 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07C323-22
ICS A61K031-16; A61K031-19; A61K031-215; A61K031-275; A61K031-34; A61K031-38; A61K031-395; A61K031-40; A61K031-415; A61K031-44; A61K031-445; A61K031-535; A61K031-55; A61K031-575; C07C323-52; C07C323-54; C07D207-325; C07D209-18; C07D213-30
CC 1-8 (Pharmacology)
Section cross-reference(s): 23, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

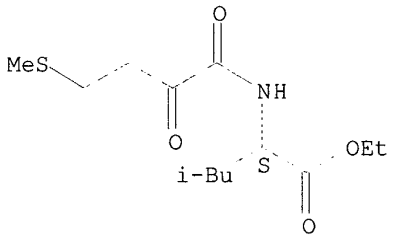
PI JP 06316557 A2 19941115 JP 1994-60035 19940304 <--
PRAI JP 1993-71210 19930306 <--
OS MARPAT 122:151382
AB Novel alkylthiofatty acid derivs. (4-alkylthio-2-oxobutanoic acids, 4-alkylthio-2-hydroxy-2-butanoic acids, 4-alkylthio-2-hydroxybutenoic acids) are prepd. and used in treating liver, kidney, pancreas, and **brain** diseases. Thus, 4-methylthio-2-oxobutanoic acid and cyclohexylmethanol were reacted to form cyclohexylmethyl 4-methylthio-2-oxobutanoate. The compd. administered orally to mice with .alpha.-naphthylisothiocyanate-induced liver damage markedly lowered the blood GOT, GPT and LAP levels, indicating a therapeutic effect. Tablets were formulated contg. the compd. 25, lactose 60, corn starch 40, polyvinyl alc. 2, and magnesium stearate 1 mg.
ST alkylthiofatty acid liver kidney disease; pancreas disease alkylthiofatty acid; **brain** disease alkylthiofatty acid
IT Poisoning
(liver; prepn. of alkylthiofatty acid derivs. and their uses in treating liver, kidney, pancreas, and **brain** diseases)
IT Anxiety
Brain, disease
Cirrhosis
Gout
Hepatitis
Kidney, disease
Liver, disease
Pancreas, disease
Parkinsonism
(prepn. of alkylthiofatty acid derivs. and their uses in treating liver, kidney, pancreas, and **brain** diseases)
IT **Mental disorder**
(depression, prepn. of alkylthiofatty acid derivs. and their uses in treating liver, kidney, pancreas, and **brain** diseases)
IT Kidney, disease
(failure, acute, prepn. of alkylthiofatty acid derivs. and their uses in treating liver, kidney, pancreas, and **brain** diseases)
IT Liver, disease
(fatty, prepn. of alkylthiofatty acid derivs. and their uses in treating liver, kidney, pancreas, and **brain** diseases)
IT 69-93-2, Uric acid, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(metabolic disorder, hyperuricemia; prepn. of alkylthiofatty acid derivs. and their uses in treating liver, kidney, pancreas, and **brain** diseases)
IT 49540-17-2P 52703-96-5P 107969-81-3P 161192-78-5P 161192-79-6P
161192-80-9P 161192-81-0P 161192-82-1P 161192-83-2P 161192-84-3P
161192-85-4P 161192-86-5P 161192-87-6P 161192-88-7P 161192-89-8P
161192-90-1P 161192-91-2P 161192-92-3P 161192-93-4P 161192-94-5P
161192-95-6P 161192-96-7P 161192-97-8P 161192-98-9P 161192-99-0P
161193-00-6P 161193-01-7P 161193-02-8P 161193-03-9P 161193-04-0P
161193-05-1P 161193-06-2P 161193-07-3P 161193-08-4P 161193-09-5P
161193-10-8P 161193-11-9P **161193-12-0P** 161193-13-1P
161193-14-2P 161193-15-3P 161193-16-4P 161193-17-5P 161193-18-6P
161193-19-7P 161193-20-0P 161193-21-1P 161193-22-2P 161193-23-3P
161193-24-4P 161193-25-5P 161193-26-6P 161193-27-7P 163549-29-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of alkylthiofatty acid derivs. and their uses in treating liver, kidney, pancreas, and **brain** diseases)
IT 100-49-2, Cyclohexylmethanol 100-55-0, 3-Pyridylcarbinol 100-79-8, 2,3-O-Isopropylidene glycerol 111-26-2, Hexylamine 142-62-1, n-Caproic acid, reactions 504-24-5, 4-Aminopyridine 583-03-9, 1-Phenylpentanol 583-91-5, 2-Hydroxy-4-methylthiobutanoic acid 583-92-6,

4-Methylthio-2-oxobutanoic acid 586-95-8, 4-Pyridylcarbinol 586-98-1, 2-Pyridylcarbinol 591-81-1, 4-Hydroxybutanoic acid 629-11-8, 1,6-Hexanediol 638-45-9, 1-Iodohexane 1152-62-1, N-Benzyloxycarbonylmethionine 2488-15-5 3569-99-1, N-(Hydroxymethyl)nicotinamide 7524-50-7, L-Phenylalanine methyl ester hydrochloride 10065-72-2, L-Alanine methyl ester 84688-35-7 161193-28-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of alkylthiofatty acid derivs. and their uses in treating liver, kidney, pancreas, and **brain** diseases)

IT **161193-12-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of alkylthiofatty acid derivs. and their uses in treating liver, kidney, pancreas, and **brain** diseases)

RN 161193-12-0 HCAPLUS
CN L-Leucine, N-[4-(methylthio)-1,2-dioxobutyl]-, ethyl ester (9CI) (CA INDEX NAME)

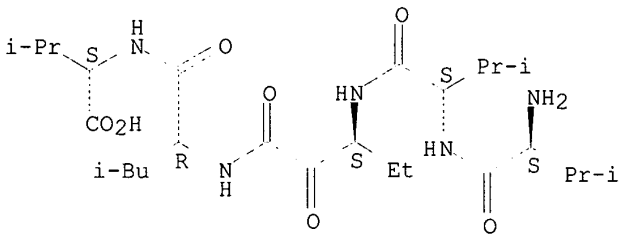
Absolute stereochemistry.



L141 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:573417 HCAPLUS
DN 119:173417
TI Prolyl endopeptidase inhibitors
AU Aoyagi, Takaaki; Muraoka, Yasuhiko
CS Showa Coll. Pharm. Sci., Machida, 194, Japan
SO Tanpakushitsu Kakusan Koso (**1993**), 38(11), 1971-86
CODEN: TAKKAJ; ISSN: 0039-9450
DT Journal; General Review
LA Japanese
CC 1-0 (Pharmacology)
AB A review with 81 refs. on prolyl endopeptidase (PEP) and its inhibitors, poststatins. It had been found that PEP activity was increased in spleen of systemic lupus erythematosus model animal and **brain** tissue of **Alzheimer**'s disease (AD). Properties of PEP, gradual changes of enzyme activity in spleen of control mouse DBA/Z and hybrid mouse NZB/W, correlation between PEP activity and Pro-IP activity in each organ or in spleen are described. Changes in **brain** or in serum protease activity of AD are also described. Structure and activity of postatin, an inhibitor of PEP isolated from S. viridochromogenes, and its analog are summarized.
ST review prolyl endopeptidase inhibitor poststatin; erythematosus **Alzheimer** disease treatment review
IT Lupus erythematosus
(treatment of, poststatins for, as prolyl endopeptidase inhibitors)
IT **Mental disorder**
(**Alzheimer**'s disease, treatment of, poststatins for, as prolyl endopeptidase inhibitors)
IT **135219-43-1D**, Poststatin, derivs.

RL: BIOL (Biological study)
(for treatment of systemic lupus erythematosus and **Alzheimer**'s disease, as prolyl endopeptidase inhibitors)
IT 72162-84-6, Prolyl endopeptidase
RL: BIOL (Biological study)
(inhibitors of, poststatins as, for treatment of systemic lupus erythematosus and **Alzheimer**'s disease)
IT **135219-43-1D**, Poststatin, derivs.
RL: BIOL (Biological study)
(for treatment of systemic lupus erythematosus and **Alzheimer**'s disease, as prolyl endopeptidase inhibitors)
RN 135219-43-1 HCAPLUS
CN L-Valine, L-valyl-L-valyl-(3S)-3-amino-2-oxopentanoyl-D-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:496186 HCAPLUS
DN 119:96186
TI Preparation of pseudopeptides and dipeptides characterized by a substituted methyl ketone moiety at the C-terminus as thiol protease inhibitors
IN Ando, Ryoichi; Ando, Naoko; Masuda, Hirokazu; Morinaka, Yasuhiro; Takahashi, Chizuko; Tamao, Yoshikuni; Tobe, Akihiro
PA Mitsubishi Kasei Corp., Japan
SO Eur. Pat. Appl., 218 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07D307-56
ICS C07D307-84; C07D307-85; C07D307-68; C07D307-38; C07D307-42; C07D307-52; C07D213-32; C07D235-06; C07D261-08; C07D263-20; C07D277-26; C07D295-125; C07D405-12; C07D407-12; C07D409-12; C07C271-54; C07C317-28; C07C323-41; C07K005-06
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 525420	A1	19930203	EP 1992-111129	19920701	<--
	EP 525420	B1	19990512			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE					
	JP 05246968	A2	19930924	JP 1992-165094	19920623	<--
	JP 3190431	B2	20010723			
	CA 2072834	AA	19930102	CA 1992-2072834	19920630	<--
	AT 179974	E	19990515	AT 1992-111129	19920701	<--
	ES 2132096	T3	19990816	ES 1992-111129	19920701	<--
	US 5639783	A	19970617	US 1995-451720	19950526	<--
	US 5834508	A	19981110	US 1997-798036	19970206	<--
PRAI	JP 1991-160674	A	19910701	<--		

JP 1991-277905 A 19911024 <--
JP 1991-343668 A 19911225 <--
US 1992-907228 B1 19920701 <--
US 1994-252397 B1 19940601 <--
US 1995-451720 A3 19950526 <--

OS MARPAT 119:96186

AB R1(NR2CHR3CO)nNR4CHR5CONR6CR7R8COCH2AR9 [R1 = H, R10CO, R10O2C, R10SO2, R10NHCO; R2; R4, R6 = H, alkyl; R3, R5 = alkoxy, H, aralkoxy, (substituted) aryl, alkyl; R2R3, R4R5 = (substituted) heterocyclyl; R7 = H, (substituted) alkyl, aralkoxy, aryl, alkoxy; R8 = H, alkyl, (substituted) aralkyl; R7R8 = (substituted) benzylidene, cycloalkyl; A = S, SO, SO2, O, NH, alkylimino; R9 = H, (substituted) aryl, (CH2)nX; n = 0, 1; m = 0-15; X = H, OH, alkylthio, alkoxycarbonylamino, (substituted) heterocyclyl, amino, arylamino, halo, alkoxy, (substituted) aryl, aryloxy; R10 = (substituted) alkyl], were prepd. Thus, S-3-amino-1-furfurylthio-2-heptanone hydrochloride (prepn. given) was condensed with tert-butoxycarbonylleucine N-hydroxysuccinimido ester in CH2Cl2 contg. Et3N to give 96% S-3-(S-2-tert-butoxycarbonylamino-4-methylvalerylamino)-1-furfurylthio-2-heptanone. This inhibited papain, cathepsin B, cathepsin L, and m-calpain with IC50's of 0.37, 0.057, 0.038, and 5.8 .mu.m, resp. Dosage forms were prepd. contg. specific title compds.

ST peptide analog thiol protease inhibitor; methyl ketone peptide protease inhibitor; cathepsin inhibitor peptide methyl ketone; muscular dystrophy treatment peptide analog; amyotrophy treatment peptide analog; ischemic disease treatment peptide analog; multiple sclerosis treatment peptide analog; cancer treatment peptide analog

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(Me ketone derivs., prepn. of, as thiol protease inhibitors)

IT Allergy inhibitors
Blood platelet aggregation inhibitors
Inflammation inhibitors
Neoplasm inhibitors
(peptide Me ketone derivs.)

IT Multiple sclerosis
Muscular dystrophy
(treatment of, peptide Me ketone derivs.)

IT Cataract
Hepatitis
Ischemia
(treatment of, peptide Me ketone derivs. for)

IT Prostate gland
(disease, hyperplasia, treatment of, of peptide Me ketone derivs. for)

IT Heart, disease
(infarction, treatment of, peptide Me ketone derivs.)

IT Liver, disease
(necrosis, treatment of, peptide Me ketone derivs. for)

IT **Nerve, disease**
(**neuropathy**, treatment of, peptide Me ketone derivs. for)

IT Hormones
RL: USES (Uses)
(sex, receptors, abnormal activation of, treatment of, peptide Me ketone derivs. for)

IT **Brain, disease**
(**stroke**, treatment of, peptide Me ketone derivs.)

IT 9001-73-4, Papain 9047-22-7, Cathepsin B 37353-41-6, Thiol protease 60616-82-2, Cathepsin L
RL: USES (Uses)
(inhibitors, peptide Me ketone derivs.)

IT 78990-62-2, Calpain
RL: RCT (Reactant); RACT (Reactant or reagent)
(m-, inhibitors, peptide Me ketone derivs.)

IT 149025-90-1P 149045-29-4P 149045-30-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for peptide Me ketone deriv. thiol protease inhibitor)

IT 149043-05-0P 149043-06-1P 149043-07-2P 149043-08-3P 149043-09-4P
149043-10-7P 149043-11-8P 149043-12-9P 149043-13-0P 149043-14-1P
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149045-07-8P 149045-08-9P 149045-09-0P 149045-10-3P 149045-11-4P
149045-12-5P 149045-13-6P 149045-14-7P 149045-15-8P 149045-16-9P
149045-17-0P 149045-18-1P 149045-19-2P 149045-20-5P 149045-21-6P
149045-22-7P 149045-23-8P **149045-24-9P** 149045-25-0P
149045-26-1P 149045-27-2P 149045-28-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as thiol protease inhibitor)

IT 98-02-2, 2-Furanmethanethiol 149045-31-8

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of peptide Me ketone deriv. thiol protease inhibitor)

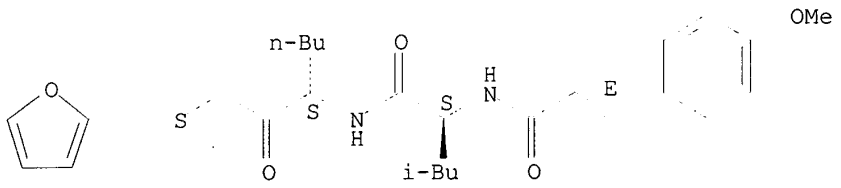
IT **149043-88-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as thiol protease inhibitor)

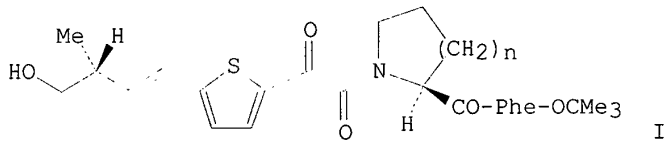
RN 149043-88-9 HCAPLUS

CN Pentanamide, N-[1-[[(2-furanylmethyl)thio]acetyl]pentyl]-2-[[3-(4-methoxyphenyl)-1-oxo-2-propenyl]amino]-4-methyl-, [S-[R*,R*-(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L141 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:22591 HCAPLUS
DN 118:22591
TI Design and synthesis of novel **FKBP** inhibitors
AU Hauske, James R.; Dorff, Peter; Julin, Susan; DiBrino, Joseph; Spencer, Robin; Williams, Rebecca
CS Cent. Res., Div. Pfizer Inc., Groton, CT, 06340, USA
SO Journal of Medicinal Chemistry (**1992**), 35(23), 4284-96
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 26
GI



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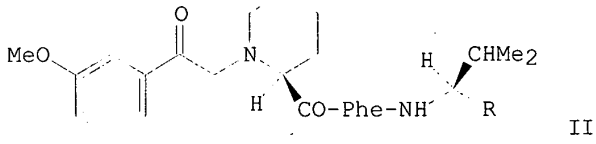


II

AB Small mol. **FK-506 binding protein** (**FKBP**) inhibitors, e.g. I (n = 1, 2) and II (R = CO-Phe-OMe, trans-CH:CHCH2O2CCF3, trans-CH:CICH2O2CCF3) were prepd. with inhibitory activity ranging from micromolar to nanomolar. The design of these inhibitors derives from a structural anal. of the substrates for **FKBP** and cyclophilin. As a consequence of this anal. two key observations were made, namely: (1) aminoketone moieties are suitable as **FKBP recognition** elements at the P1-P12 site, and (2) the P32-P42 site will accept a trans-olefin as a suitable mimetic of a peptide moiety. The prepn. of these nonpeptide inhibitors is readily accomplished by a protocol which includes the synthesis of chiral propargylic amines and their subsequent conversion into vinyl zirconium reagents.
ST **FK 506 binding protein** inhibitor; cyclophilin inhibitor structure activity; aminoketone peptide isostere **immunophilin** inhibitor; pseudopeptide alkene **immunophilin** inhibitor
IT Molecular structure-biological activity relationship

(**FK-506 binding protein**
inhibitory, of small mols. contg. aminoketone and alkene dipeptide isosteres)

IT Proteins, specific or class
RL: RCT (Reactant); RACT (Reactant or reagent)
(FK-506 binding, inhibitors, small mols. contg. aminoketone and alkene dipeptide isosteres)

IT **Proteins, specific or class**
RL: USES (Uses)
(**immunophilins**, inhibitors, small mols. contg. aminoketone and alkene dipeptide isosteres)

IT 3393-45-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(Michael addn. reaction of, with vinylzirconium reagent, nickel-promoted)

IT 98-03-3, 2-Thiophenecarboxaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(Wittig olefination of, with [hydroxy(methyl)propyl]triphenylphosphonium salt)

IT 73805-15-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(Wittig olefination of, with thiophenecarboxaldehyde)

IT 311-46-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(Wittig reaction of, with valinal deriv.)

IT 27491-70-9, Dimethyl (diazomethyl)phosphonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(Wittig reaction of, with valinal deriv., acetylene deriv. from)

IT 5781-53-3, Methyl oxalyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by, of proline and pipecolinic acid derivs.)

IT 2812-46-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of, with Me oxalyl chloride)

IT 613-54-7, 2-(Bromoacetyl)naphthalene 5000-65-7 118388-72-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of proline and pipecolinic acid derivs. in prepn. of **FK-506 binding protein** inhibitors)

IT 2677-37-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, with (bromomethyl)arene derivs. in prepn. of **FK-506 binding protein** inhibitors)

IT 13734-41-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with dimethylhydroxylamine)

IT 2627-86-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with vinylogous valine deriv.)

IT **145037-65-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with lithiothiophene deriv. in prepn. of **FK-506 binding protein** inhibitor)

IT 145037-68-9
RL: PROC (Process)
(conversion of, to bromomethylketone deriv.)

IT 79069-51-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(olefination of, with phosphonoacetate or (diazomethyl)phosphonate)

IT 145037-75-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, (bromoacetyl)naphthalene, in prepn. of **FK-506 binding protein** inhibitor)

IT 26250-84-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with nitrophenylalanine ester)
IT 28697-11-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with phenylalanine ester)
IT 16874-17-2, Phenylalanine tert-butyl ester 116366-32-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with pipecolinic acid deriv.)
IT **145021-17-6P 145021-19-8P** 145021-20-1P 145021-21-2P
145021-22-3P 145021-23-4P **145021-24-5P** 145021-25-6P
145021-26-7P 145021-27-8P 145021-28-9P 145021-29-0P 145021-30-3P
145021-31-4P 145021-32-5P 145021-33-6P 145021-34-7P 145021-35-8P
145021-36-9P 145021-37-0P 145021-38-1P 145021-39-2P 145021-40-5P
145021-41-6P 145021-42-7P 145021-43-8P 145021-46-1P 145021-47-2P
145021-48-3P 145021-49-4P 145021-50-7P 145021-51-8P 145021-52-9P
145021-53-0P 145021-54-1P 145021-55-2P 145021-56-3P 145021-57-4P
145021-58-5P 145021-59-6P 145021-60-9P 145021-61-0P 145021-62-1P
145021-63-2P 145021-64-3P 145021-65-4P 145021-66-5P 145021-67-6P
145021-68-7P 145037-51-0P 145107-46-6P 145107-47-7P 145108-13-0P
145108-14-1P 145108-15-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and **FK-506 binding protein** inhibitory activity of)
IT 145037-73-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and Hofmann elimination of, allylalanine deriv. from)
IT 145037-53-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and acylation of, with Me oxalyl chloride)
IT 145037-67-8P 145037-69-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation by, of proline and pipecolinic acid derivs. in prepn. of **FK-506 binding protein** inhibitors)
IT 145037-52-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and catalytic hydrogenolysis of)
IT **145037-54-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with lithiothiophene deriv.)
IT **141084-09-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with lithiothiophene deriv. in prepn. of **FK-506 binding protein** inhibitor)
IT 145037-66-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to bromomethyl ketone deriv.)
IT 145037-56-5P 145037-57-6P 145037-58-7P 145037-70-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deblocking of, with hydrogen chloride)
IT **145037-55-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and desilylation of)
IT 104700-38-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydride redn. of, alc. from)

IT 143327-88-2P 143327-89-3P 143327-90-6P 143327-91-7P 143327-92-8P
143327-93-9P 145037-59-8P 145037-60-1P 145037-61-2P 145037-62-3P
145037-71-4P 145037-74-7P 145037-76-9P 145037-77-0P 145037-78-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and peptide coupling reactions of, in prepn. of **FK-506 binding protein** inhibitor)

IT 145037-63-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and silylation of)

IT 145037-72-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and N-oxidn. of)

IT 143327-85-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 87694-52-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., Grignard benzylation, or hydride redn. of)

IT 104700-44-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., acylation, and etherification reactions of)

IT 145021-45-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., deblocking, and **FK-506 binding protein** inhibitory activity of)

IT **145021-16-5P 145021-18-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., desilylation, and **FK-506 binding protein** inhibitory activity of)

IT 143327-78-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., hydrozirconation, and addn. reactions of, with Michael acceptors, nickel-promoted)

IT 145037-64-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., lithiation, and condensation of, with oxalate esters or chloroforamate)

IT 145021-44-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., N-alkylation, and **FK-506 binding protein** inhibitory activity of)

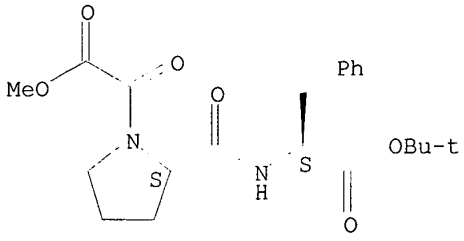
IT 7750-42-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive methylation of, di-Me deriv. from)

IT 104987-11-3, FK-506
RL: RCT (Reactant); RACT (Reactant or reagent)
(small mols. contg. aminoketone and alkene dipeptide isosteres as mimics of)

IT **145037-65-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with lithiothiophene deriv. in prepn. of **FK-506 binding protein** inhibitor)

RN 145037-65-6 HCAPLUS
CN L-Phenylalanine, N-[1-(methoxyoxoacetyl)-L-prolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

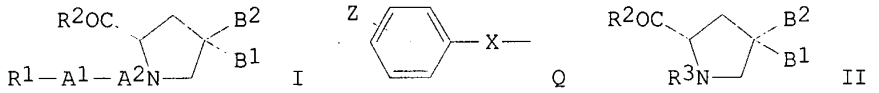
Absolute stereochemistry.



L141 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1989:633680 HCAPLUS
DN 111:233680
TI Preparation of tripeptides containing L-proline derivatives as nootropics and pharmaceutical compositions containing them
IN Fiez-Vandal, Pierre Yves
PA Inorgan S. A., Switz.
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA French
IC ICM C07K005-08
ICS A61K037-02
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 316218	A1	19890517	EP 1988-402761	19881103	<--
	EP 316218	B1	19930915			
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	FR 2622581	A1	19890505	FR 1987-15228	19871103	<--
	FR 2622581	B1	19900216			
	JP 01157998	A2	19890621	JP 1988-276343	19881102	<--
	FI 8805083	A	19890504	FI 1988-5083	19881103	<--
	US 5212158	A	19930518	US 1988-266680	19881103	<--
	AT 94560	E	19931015	AT 1988-402761	19881103	<--
	ES 2061710	T3	19941216	ES 1988-402761	19881103	<--
	KR 121793	B1	19971127	KR 1988-14433	19881103	<--
	CA 1340227	A1	19981215	CA 1988-582169	19881103	<--
PRAI	FR 1987-15228	A	19871103	<--		
	EP 1988-402761	A	19881103	<--		

OS CASREACT 111:233680; MARPAT 111:233680
GI



AB The title compds. [I; R1 = Q; X = CO, YCO, OYCO; Y = alkylene, alkenylene; Z = H, .gtoreq.1 CF3, alkyl, alkylenedioxy; R2 = NH2, OH, or a functional deriv. thereof; A1, A2 = amino acid residue; B1, B2 = H, Me] and their pharmaceutically acceptable salts, useful as nootropics for treatment of senile dementia, **Alzheimer**'s disease, **Parkinson**'s disease, schizophrenia, and depression, are prepd. via reaction of

activated R1-A1-OH with proline derivs. II (R3 = H-A2), obtained by reaction of II (R3 = H) with activated H-A2-OH. N-Cinnamoylglycine (prepn. given) was condensed with II.CF3CO2H (R2 = NH2, B1 = B2 = H, R3 = H-Phe)(prepn. given) in DMF contg. dicyclohexylcarbodiimide and N-methylmorpholine to give I (R1 = cinnamoyl, R2 = NH2, B1 = B2 = H, A1 = Gly, A2 = Phe) (III). III, administered i.p. or p.o. at 1 mg/kg, was effective in antagonizing scopolamine-induced amnesia in mice.

ST proline contg tripeptide prepn nootropic

IT Antidepressants
(proline-contg. peptides)

IT **Parkinsonism**
Schizophrenia
(treatment of, proline-contg. tripeptides for)

IT **Mental disorder**
(**Alzheimer**'s disease, treatment of, proline-contg. tripeptides for)

IT Psychotropics
(psychoanaleptics, proline-contg. tripeptides)

IT **Mental disorder**
(senile psychosis, treatment of, proline-contg. tripeptides for)

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(tri-, proline-contg., prepn. of, as nootropics)

IT 495-69-2P 500-98-1P 16534-24-0P 19811-56-4P **40778-04-9P**
52386-67-1P 69470-09-3P 105443-86-5P 105443-87-6P 105624-42-8P
111574-12-0P 123910-59-8P **123910-60-1P** 123910-61-2P
123910-62-3P 123910-63-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for nootropic peptides)

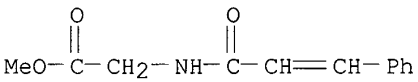
IT **123910-50-9P** 123910-51-0P **123910-52-1P**
123910-53-2P 123910-54-3P 123910-55-4P **123910-56-5P**
123910-57-6P **123910-58-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as nootropic)

IT 65-85-0, Benzoic acid, reactions 90-50-6, 3,4,5-Trimethoxycinnamic acid 102-92-1, Cinnamoyl chloride 103-82-2, Phenylacetic acid, reactions 459-32-5, 4-Fluorocinnamic acid 2373-80-0, 3,4-(Methylenedioxy)cinnamic acid 2812-47-7, Prolinamide 5680-79-5, Glycine methyl ester hydrochloride 13139-15-6 13734-34-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of nootropic peptides)

IT **40778-04-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for nootropic peptides)

RN 40778-04-9 HCAPLUS

CN Glycine, N-(1-oxo-3-phenyl-2-propenyl)-, methyl ester (9CI) (CA INDEX NAME)



L141 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2003 ACS

AN 1989:423387 HCAPLUS

DN 111:23387

TI Preparation of 3-indolepyruvic acid derivatives and pharmaceutical use thereof

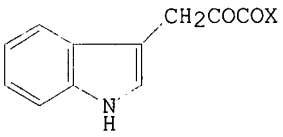
IN De Luca, Giovanna; Di Stazio, Giovanni; Margonelli, Andrea; Materazzi, Mario; Politi, Vincenzo

PA Polifarma S.p.A., Italy

SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D209-18
ICS A61K031-405
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8809789	A2	19881215	WO 1988-IT41	19880601 <--
	WO 8809789	A3	19890209		
	W: AU, BR, DK, FI, JP, KR, NO, US				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	CA 1328658	A1	19940419	CA 1988-567675	19880525 <--
	AU 8819433	A1	19890104	AU 1988-19433	19880601 <--
	AU 609500	B2	19910502		
	EP 321516	A1	19890628	EP 1988-904984	19880601 <--
	EP 321516	B1	19930303		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 02500369	T2	19900208	JP 1988-504630	19880601 <--
	AT 86247	E	19930315	AT 1988-904984	19880601 <--
	NO 8900408	A	19890330	NO 1989-408	19890201 <--
	FI 8900508	A	19890202	FI 1989-508	19890202 <--
	FI 92055	B	19940615		
	FI 92055	C	19940926		
	DK 8900467	A	19890331	DK 1989-467	19890202 <--
	DK 170438	B1	19950904		
	US 5002963	A	19910326	US 1989-327804	19890203 <--
PRAI	IT 1987-48014		19870603 <--		
	EP 1988-904984		19880601 <--		
	WO 1988-IT41		19880601 <--		

OS MARPAT 111:23387
GI



I

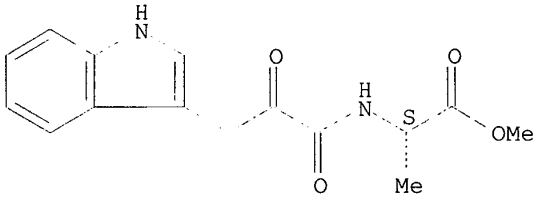
AB The title compds. [I; X = C1-4 alkoxy, cyclohexyloxy, PhCH2O, C1-4 (di)alkylamino, (di)cyclohexylamino, PhCH2NH, (PhCH2)2N, amino acid residue], useful as central **nervous** system (CNS) agents, are prepd. Hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl were added to a soln. of I (X = OH) in THF under Ar and cooling, followed by Me2NH.HCl and 4-methylmorpholine to give 35% amide I (X = Me2N). In an audiogenic convulsion test, I (X = OH) and its Mg salt showed 33% and 29% convulsion rate, resp., at 200 mg/kg, i.v. in mice, vs. 80% with tryptophan and 65% with controls. I also protected against N-methyl-D-aspartic acid-induced convulsion at 1 g/kg i.p. in mice, with a death rate of 3/9, vs. 8/10 of controls.

ST indolepyruvic acid prepn CNS agent; epilepsy treatment indolepyruvic acid prepn; ictus treatment indolepyruvic acid prepn; **Alzheimer** treatment indolepyruvic acid prepn; cerebral ischemia treatment indolepyruvic acid prepn; ischemia cerebral treatment indolepyruvic acid prepn

IT Anticonvulsants and Antiepileptics
Nervous system agents

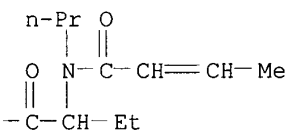
(indolepyruvic acid derivs.)
IT **Mental disorder**
(**Alzheimer**'s disease, treatment of, indolepyruvic acid derivs. for)
IT **Brain, disease or disorder**
(**ischemia**, treatment of, indolepyruvic acid derivs. for)
IT 392-12-1P 7417-64-3P 32817-17-7P 66872-76-2P 121306-89-6P
121306-90-9P 121306-91-0P 121306-92-1P 121306-93-2P 121306-94-3P
121306-95-4P 121306-96-5P 121306-97-6P 121306-98-7P 121306-99-8P
121307-00-4P 121307-01-5P 121307-02-6P 121307-03-7P 121307-04-8P
121307-05-9P 121307-06-0P 121307-07-1P 121307-08-2P 121307-09-3P
121307-10-6P 121307-11-7P 121307-12-8P
121307-13-9P 121307-14-0P 121307-15-1P
121307-16-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as central **nervous** system agent)
IT 392-12-1DP, 3-Indolepyruvic acid, derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as central **nervous** system agents)
IT **121307-10-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as central **nervous** system agent)
RN 121307-10-6 HCAPLUS
CN L-Alanine, N-[3-(1H-indol-3-yl)-1,2-dioxopropyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L141 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2003 ACS
AN 1971:74722 HCAPLUS
DN 74:74722
TI Effects of prethcamide, nikethamide, pentetrazole, and bemegride on central sympathetic activity and blood pressure
AU Tauberger, G.; Brus, M.
CS Pharmakol. Inst., Univ. Bonn, Bonn., Fed. Rep. Ger.
SO Anaesthesist (**1970**), 19(11), 426-32
CODEN: ANATAE; ISSN: 0003-2417
DT Journal
LA German
CC 15 (Pharmacodynamics)
GI For diagram(s), see printed CA Issue.
AB Prethcamide (I) (2.5-40 mg/kg), nikethamide (II) (2.5-80 mg/kg), pentetrazope (III) (1.75-28 mg/kg) or bemegride (IV) (0.3-10 mg/kg) i.v. injections into narcotized cats under artificial respiration increased the central sympathetic activity in a dose-dependent fashion. Analeptic drugs, I and II acting primarily via effects on the medulla differed from III and IV in that high doses of I and II increased sympathetic discharges, but decreased the blood pressure, whereas low doses of III and IV increased the blood pressure and sympathetic discharges.
ST analeptics sympathetic activity; sympathetic activity analeptics; blood pressure analeptics; prethcamide **nerves** blood pressure; nikethamide **nerves** blood pressure; pentetrazole **nerves**

blood pressure; bemegide **nerves** blood pressure
IT Blood pressure
(**nervous** system stimulants effect on)
IT **Nervous system**
(sympathetic, analeptics stimulation of)
IT 54-95-5 59-26-7 64-65-3
RL: BIOL (Biological study)
(blood pressure and sympathetic **nervous** system in response to)
IT **633-47-6**
RL: BIOL (Biological study)
(mixt with N-[1-(dimethylcarbamoyl)propyl]-N-ethylcrotonamide, blood pressure and sympathetic **nervous** system in response to)
IT **6168-76-9**
RL: BIOL (Biological study)
(mixt. with N-[1-(dimethylcarbamoyl)propyl]-N-propylcrotonamide, blood pressure and sympathetic **nervous** system in response to)
IT **633-47-6**
RL: BIOL (Biological study)
(mixt with N-[1-(dimethylcarbamoyl)propyl]-N-ethylcrotonamide, blood pressure and sympathetic **nervous** system in response to)
RN 633-47-6 HCAPLUS
CN 2-Butenamide, N-[1-[(dimethylamino)carbonyl]propyl]-N-propyl- (9CI) (CA INDEX NAME)



=> fil reg
FILE 'REGISTRY' ENTERED AT 08:17:41 ON 08 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES: 7 APR 2003 HIGHEST RN 502131-66-0
DICTIONARY FILE UPDATES: 7 APR 2003 HIGHEST RN 502131-66-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can l145

L145 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **95076-93-0** REGISTRY

CN Isomerase, peptidylprolyl cis-trans- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN E.C. 5.2.1.8
CN Parvulin
CN Parvulin 10
CN Peptide bond isomerase
CN Peptidylproline cis-trans-isomerase
CN Peptidylprolyl cis-trans-isomerase
CN Peptidylprolyl isomerase
CN **Peptidylprolyl rotamase**
CN Proline isomerase
CN **Proline rotamase**
CN Prolyl cis/trans-isomerase
CN Prolyl isomerase
CN **Rotamase**
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CHEMCATS, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
976 REFERENCES IN FILE CA (1962 TO DATE)
22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
977 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:221796

REFERENCE 2: 138:217002

REFERENCE 3: 138:215353

REFERENCE 4: 138:185019

REFERENCE 5: 138:182861

REFERENCE 6: 138:182059

REFERENCE 7: 138:167992

REFERENCE 8: 138:167734

REFERENCE 9: 138:166388

REFERENCE 10: 138:149411

=> d his

(FILE 'HOME' ENTERED AT 06:52:57 ON 08 APR 2003)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 06:53:18 ON 08 APR 2003
E ROTAMASE/CN
L1 1 S E3
E ROTAMASE
L2 40 S E3
SEL CHEM L1

FILE 'HCAPLUS' ENTERED AT 06:53:47 ON 08 APR 2003
L3 1391 S E1-E14
L4 998 S L2
E ROTAMASE
L5 173 S E3-E5

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L6          1411 S L3-L5
                 E IMMUNOPHILIN/CT
L7           100 S E7-E10
                 E E5+ALL
L8          1948 S E3,E2+NT
L9           958 S IMMUNOPHILIN?
L10         1348 S (FK506 OR FK 506)(L)(BP OR BINDING PROTEIN)
L11         1559 S FKBP?
L12         2788 S L7-L11
                 E STEINER J/AU
L13           63 S E3,E13
                 E STEINER JOE/AU
L14            3 S E3
L15          114 S E22,E24,E25
                 E HAMILTON G/AU
L16           64 S E3,E17,E18
                 E HAMILTON GREG/AU
L17          136 S E3-E6,E9,E10
                 E GUILFORD/PA,CS
                 E GUILF/PA,CS
L18          430 S E5-E40
L19          427 S GUILFORD?/PA,CS
L20            6 S (US6509477 OR US5614547)/PN
L21            4 S (US20020052410 OR US20020013344)/PN
                 E GPI/PA,CS
L22           26 S E20-E23
L23          116 S L13-L22 AND L3-L12
L24            8 S L20,L21 AND L23
L25          340 S PEPTIDYL PROLYL ISOMERASE
L26           36 S L25 AND L13-L23
L27            4 S L24 AND L26
L28            8 S L24,L27
L29          108 S L23,L26 NOT L28
L30         3504 S L6,L12,L25

     FILE 'REGISTRY' ENTERED AT 07:14:54 ON 08 APR 2003

     FILE 'HCAPLUS' ENTERED AT 07:14:54 ON 08 APR 2003
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L31           SEL L28 1- RN :     199 TERMS
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L32           199 S L31

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L33           SEL L29 1- RN :    1566 TERMS
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L34          1565 S L33

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L35           SEL L30 1- RN :   51089 TERMS
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     FILE 'REGISTRY' ENTERED AT 07:16:02 ON 08 APR 2003
L36         51089 S L35
L37         51899 S L32,L34,L36
L38               STR
L39            50 S L38
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L40       14064 S L38 FUL
                SAV TEMP L40 VKIM805/A
L41         115 S L40 AND L32
L42          84 S L32 NOT L41
L43         301 S L40 AND L34
L44         185 S L40 AND L36
L45         336 S L41,L43,L44
                SAV L45 VKIM805A/A
L46       13728 S L40 NOT L45

     FILE 'HCAPLUS' ENTERED AT 07:28:09 ON 08 APR 2003
L47         143 S L45
L48        3750 S L46
L49         119 S L47 AND L30
L50          53 S L48 AND L30
L51         145 S L49,L50
L52          66 S L47,L48 AND L13-L24,L26-L29
L53         151 S L51,L52
                E NEURON/CT
                E E4+ALL
L54        3448 S E2
                E NEURON/CT
                E E40+ALL
L55       27528 S E2
                E NEURON/CT
                E E25+ALL
L56        1757 S E2
                E NERVE/CT
                E E4+ALL
                E E4+ALL
L57      141350 S E5,E4+NT
                E E25+ALL
L58       11157 S E7,E8,E6+NT
                E E21+ALL
                E E26+ALL
L59        6157 S E9,E8+NT
                E E15+ALL
L60        4035 S E2+NT
                E E13+ALL
                E E16+ALL
L61         498 S E4+NT
                E NERVE/CT
L62      128433 S E3-E212
L63       11849 S E218 OR E219
L64        1864 S E280
L65       16330 S E308-E358
L66        9082 S E359
L67        8742 S E370-E372
L68         680 S E373
L69      275389 S E390+NT
                E E308+ALL
L70       27683 S E3+NT
                E NEUROLOG/CT
                E E5+ALL
L71       17771 S E2
                E BRAIN/CT
                E E3+ALL
L72      332934 S E4+NT
                E E53+ALL
L73      105878 S E3+NT
                E SPINE/CT
                E E3+ALL
                E E3+ALL
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L74         3096 S E9+NT
                 E E16+ALL
L75        21997 S E4+NT
L76        14129 S E8+NT
                 E STROKE/CT
                 E E3+ALL
L77         5605 S E2
                 E NEURODEGEN/CT
                 E E6+ALL
L78         4266 S E2
                 E ALZHEIMER/CT
                 E E9+ALL
L79        10981 S E6,E5+NT
L80        10748 S E23+NT OR E24+NT OR E25+NT OR E26+NT OR E27+NT OR E28+NT OR E
                 E PARKINSON/CT
L81         4331 S E12
                 E E6+ALL
L82         7744 S E3+NT OR E9+NT OR E10+NT
                 E NERVE GROWTH FACTOR/CT
                 E E3+ALL
L83         9410 S E4,E3
                 E NERVE GROWTH FACTOR/CT
                 E BRAIN DERIVED GROWTH FACTOR/CT
L84         2054 S BRAIN(L)DERIV?(L)GROWTH FACTOR
                 E NEUROTROPHIC FACTOR/CT
L85          124 S E11
                 E E6+ALL
L86         4651 S E6-E10,E5+NT
                 E E66+ALL
L87        15134 S E3-E5,E2+NT
L88         4516 S E24+NT
L89          740 S GLIAL(L)DERIV?(L)GROWTH FACTOR
L90         1529 S CILIARY(L)NEUROTROPHIC(L)FACTOR
L91         1868 S GLIAL(L)NEUROTROPHIC(L)FACTOR
L92         3617 S BRAIN(L)DERIV?(L)NEUROTROPHIC(L)FACTOR
L93        13895 S NERVE(L)GROWTH FACTOR
L94        10078 S NEUROTROPHIC(L)FACTOR
L95          409 S NEUROTROPIN 3

     FILE 'REGISTRY' ENTERED AT 07:48:22 ON 08 APR 2003
L96            1 S 130939-66-1
L97            1 S NERVE GROWTH FACTOR/CN
                 E BRAIN/CN
                 E BRAIN DERIVED/CN
L98            1 S E4
L99          260 S BRAIN (L) NEUROTROPHIC(L)(FACTOR OR PEPTIDE OR PROTEIN)
                 E GLIAL/CN
L100         194 S GLIAL (L) NEUROTROPHIC(L)(FACTOR OR PEPTIDE OR PROTEIN)
L101         180 S CILIARY (L) NEUROTROPHIC(L)(FACTOR OR PEPTIDE OR PROTEIN)

     FILE 'HCAPLUS' ENTERED AT 07:49:48 ON 08 APR 2003
L102       10104 S L96-L101
                 E PERIPHERAL NERVE/CT
                 E E3+ALL
L103        4099 S E2
L104         530 S E4
L105         727 S E6
L106        2683 S E8
L107         727 S E14
L108         727 S E18
L109          70 S L53 AND L54-95,L102-L108
L110         197 S L47,L48 AND L54-95,L102-L108
L111         278 S L53,L109,L110
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L112          92 S L111 AND (PY<=1995 OR PRY<=1995 OR AY<=1995)
L113          35 S L112 NOT P/DT
L114           7 S L113 AND L6,L25
L115          20 S L113 AND L12
L116          20 S L114,L115
L117          57 S L112 NOT L113
L118          14 S L117 AND L6,L25
L119          21 S L117 AND L12
L120          21 S L118,L119
L121          11 S L112 AND L13-L17
L122           9 S L112 AND L18,L19,L22
L123           8 S L28 AND L111
L124          41 S L116,L120-L123
L125          41 S L124 AND L3-L30,L47-L95,L102-L124
L126          15 S L125 AND (?ALZHEIM? OR ?PARKINSON? OR ?COGNIT? OR DEMENT? OR
L127          26 S L125 NOT L126
L128          11 S L121-L123
L129          11 S L128 AND L126
L130          15 S L126,L129
L131          51 S L112 NOT L124-L130
L132          12 S L131 AND (ALZHEIM? OR PARKINSON?)/CW
L133          25 S L131 AND (BRAIN, DISEASE OR NERVE, DISEASE OR NERVOUS SYSTEM
L134          28 S L132,L133
L135          10 S L134 AND (HIV OR OSTHOL OR CASSETTES OR COLLAGENASE OR CHOLEC
L136          18 S L134 NOT L135
L137          33 S L130,L136
L138          31 S L137 AND (?ALZHEIM? OR ?PARKINSON? OR ?AMYLO? OR TAU OR NEUR?
L139           2 S L137 NOT L138
L140           1 S L139 NOT CYCLOSPORIN
L141          32 S L138,L140

     FILE 'REGISTRY' ENTERED AT 08:15:03 ON 08 APR 2003

     FILE 'HCAPLUS' ENTERED AT 08:15:13 ON 08 APR 2003
               SEL HIT RN L141

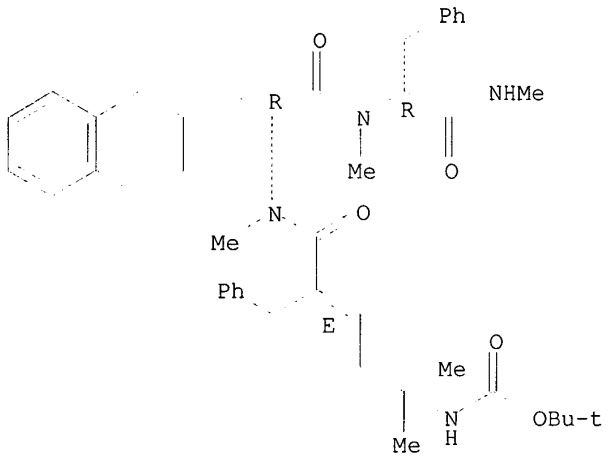
     FILE 'REGISTRY' ENTERED AT 08:16:08 ON 08 APR 2003
L142         788 S E1-E788
L143           1 S L142 AND L1
L144           1 S L142 AND L2
L145           1 S L143,L144
L146         787 S L142 NOT L145

     FILE 'REGISTRY' ENTERED AT 08:17:41 ON 08 APR 2003

=> d l146 sca

L146 787 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS
IN   D-Phenylalaninamide, N-[(2E)-5-[[(1,1-dimethylethoxy)carbonyl]amino]-5-
     methyl-1-oxo-2-(phenylmethyl)-2-hexenyl]-N-methyl-3-(2-naphthalenyl)-D-
     alanyl-N,N.alpha.-dimethyl- (9CI)
MF   C44 H54 N4 O5

Absolute stereochemistry.
Double bond geometry as shown.
```



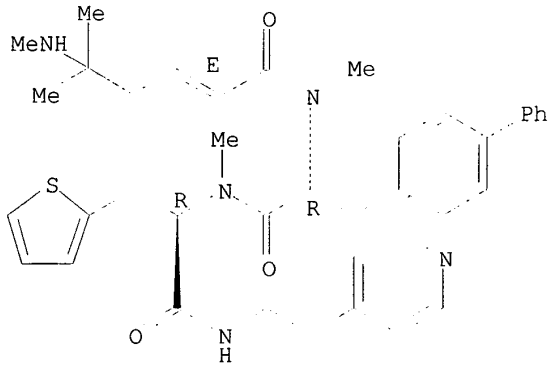
"free" view of sample cmpds from references 1-32

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):25

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Alaninamide, 3-[1,1'-biphenyl]-4-yl-N-methyl-N-[(2E)-5-methyl-5-(methylamino)-1-oxo-2-hexenyl]-D-alanyl-N2-methyl-N-[2-(4-pyridinyl)ethyl]-3-(2-thienyl)- (9CI)
MF C39 H47 N5 O3 S

Absolute stereochemistry.
Double bond geometry as shown.

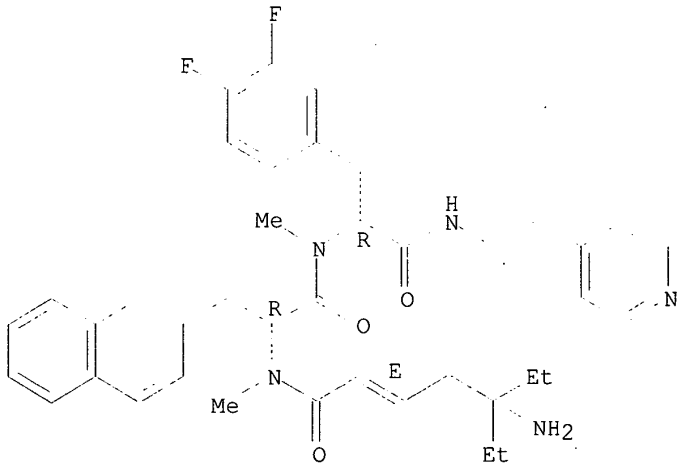


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Phenylalaninamide, N-[(2E)-5-amino-5-ethyl-1-oxo-2-heptenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-3,4-difluoro-N.alpha.-methyl-N-[2-(4-pyridinyl)ethyl]- (9CI)
MF C40 H47 F2 N5 O3

Absolute stereochemistry.

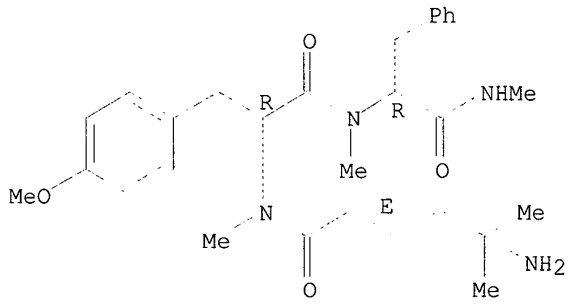
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Phenylalaninamide, N-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-N,O-dimethyl-D-tyrosyl-N,N.alpha.-dimethyl- (9CI)
MF C29 H40 N4 O4

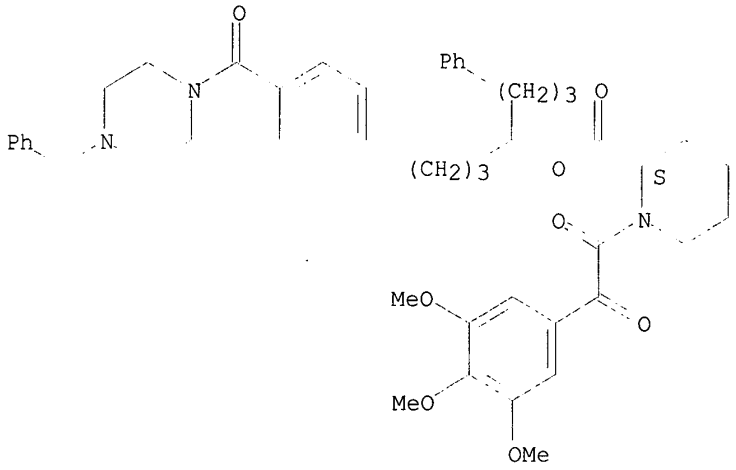
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-[4-[[4-(phenylmethyl)-1-piperazinyl]carbonyl]phenyl]-1-(3-phenylpropyl)butyl ester, (2S)- (9CI)
MF C48 H57 N3 O8

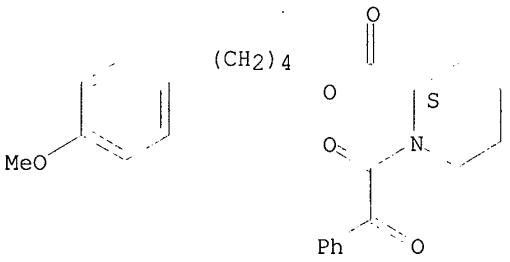
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, 4-(4-methoxyphenyl)butyl ester, (2S)- (9CI)
MF C25 H29 N O5

Absolute stereochemistry.

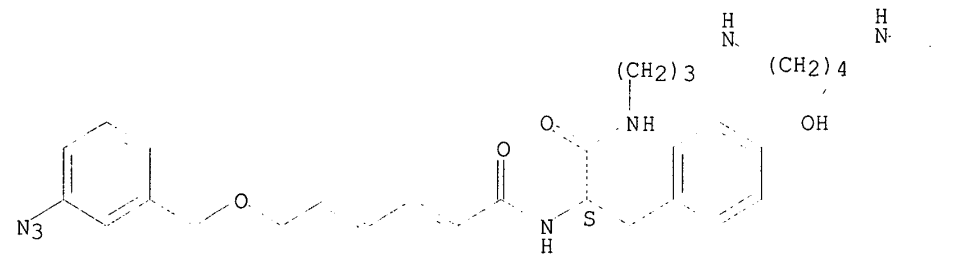


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

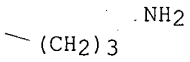
L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Benzenepropanamide, N-[3-[[4-[(3-aminopropyl)amino]butyl]amino]propyl]-.alpha.-[[6-[(3-azidophenyl)methoxy]-1-oxo-2,4-hexadienyl]amino]-4-hydroxy-, (S)- (9CI)
MF C32 H46 N8 O4

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A

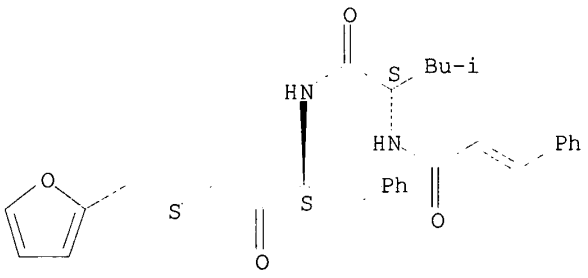


PAGE 1-B



L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Pentanamide, N-[3-[(2-furanylmethyl)thio]-2-oxo-1-(phenylmethyl)propyl]-4-methyl-2-[(1-oxo-3-phenyl-2-propenyl)amino]-, [S-(R*,R*)]- (9CI)
MF C30 H34 N2 O4 S

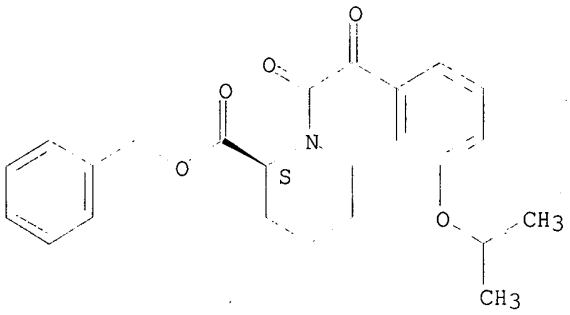
Absolute stereochemistry.
Double bond geometry unknown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxylic acid, 1-[[3-(1-methylethoxy)phenyl]oxoacetyl]-, phenylmethyl ester, (S)- (9CI)
MF C24 H27 N O5

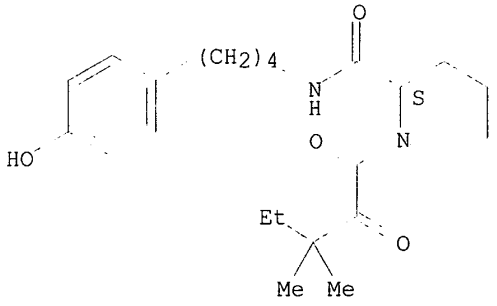
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxamide, 1-(3,3-dimethyl-1,2-dioxopentyl)-N-[4-(4-hydroxyphenyl)butyl]-, (2S)- (9CI)
MF C23 H34 N2 O4

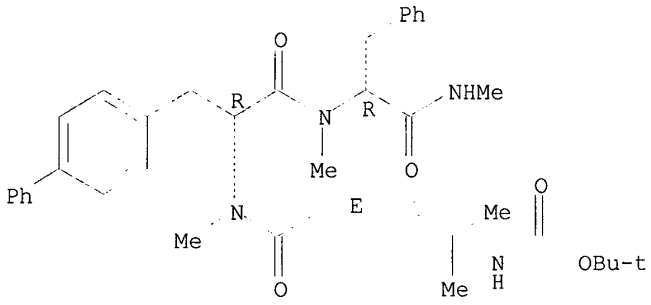
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Phenylalaninamide, 3-[1,1'-biphenyl]-4-yl-N-[(2E)-5-[[(1,1-dimethylethoxy)carbonyl]amino]-5-methyl-1-oxo-2-hexenyl]-N-methyl-D-alanyl-N,N.alpha.-dimethyl- (9CI)
MF C39 H50 N4 O5

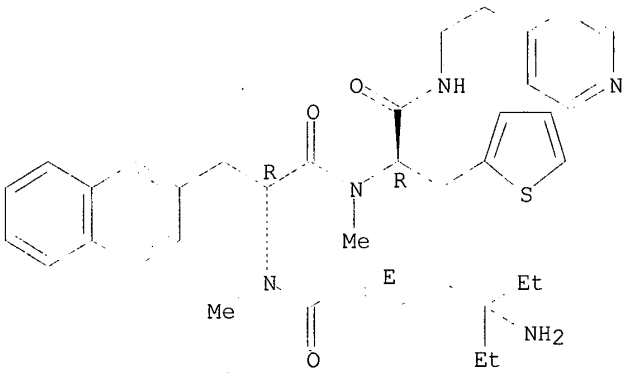
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Alaninamide, N-[(2E)-5-amino-5-ethyl-1-oxo-2-heptenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N2-methyl-N-[2-(4-pyridinyl)ethyl]-3-(2-thienyl)-(9CI)
MF C38 H47 N5 O3 S

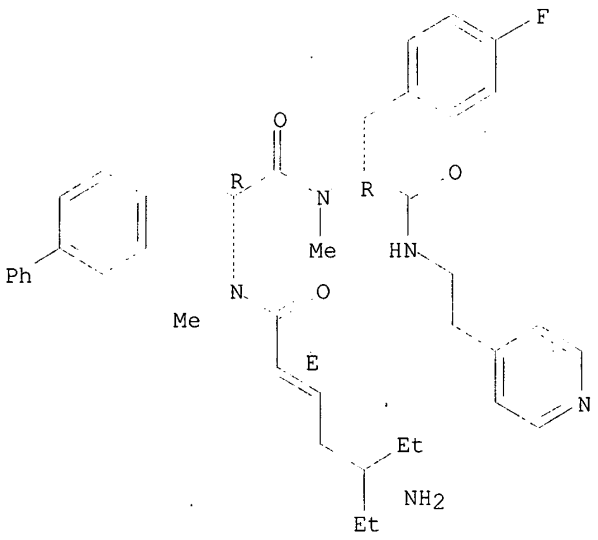
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Phenylalaninamide, N-[(2E)-5-amino-5-ethyl-1-oxo-2-heptenyl]-3-[1,1'-biphenyl]-4-yl-N-methyl-D-alanyl-4-fluoro-N.alpha.-methyl-N-[2-(4-pyridinyl)ethyl]- (9CI)
MF C42 H50 F N5 O3

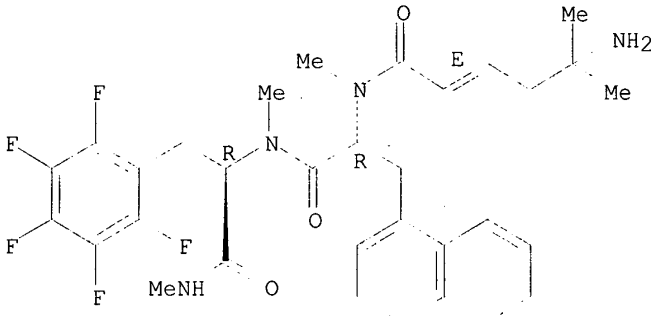
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Phenylalaninamide, N-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-N-methyl-3-(1-naphthalenyl)-D-alanyl-2,3,4,5,6-pentafluoro-N,N.alpha.-dimethyl- (9CI)
MF C32 H35 F5 N4 O3

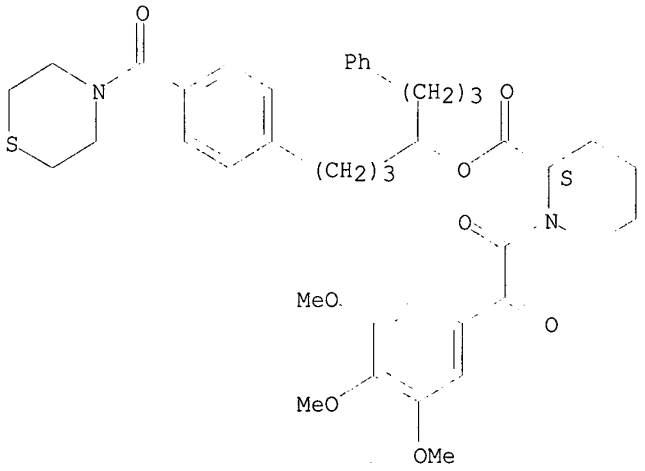
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 1-(3-phenylpropyl)-4-[4-(4-thiomorpholinylcarbonyl)phenyl]butyl ester, (2S)- (9CI)
MF C41 H50 N2 O8 S

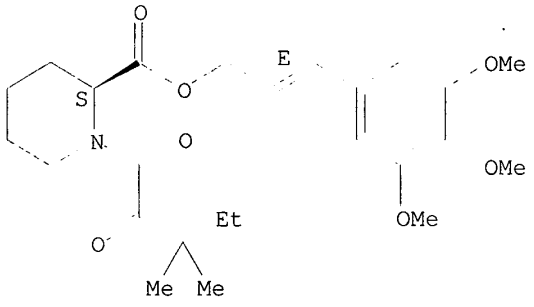
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

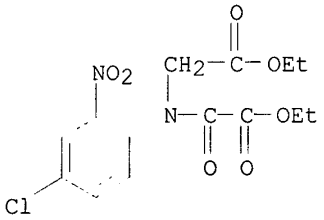
L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxylic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)-, (2E)-3-(3,4,5-trimethoxyphenyl)-2-propenyl ester, (2S)- (9CI)
MF C25 H35 N O7

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Glycine, N-(4-chloro-2-nitrophenyl)-N-(ethoxyoxoacetyl)-, ethyl ester (9CI)
MF C14 H15 Cl N2 O7

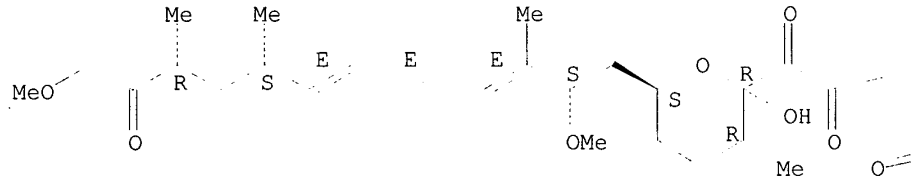


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

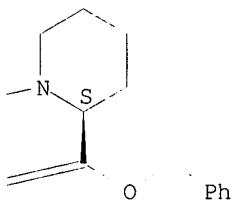
L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, phenylmethyl ester, (2S)- (9CI)
MF C39 H55 N O9

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



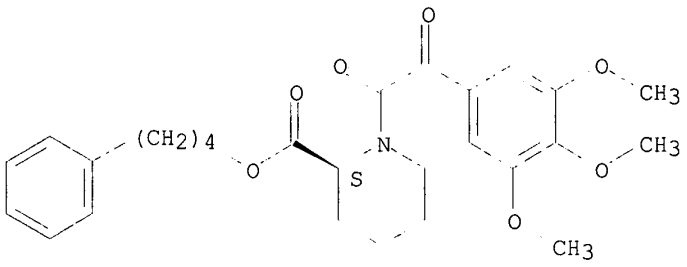
PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-phenylbutyl ester, (2S)- (9CI)
MF C27 H33 N O7

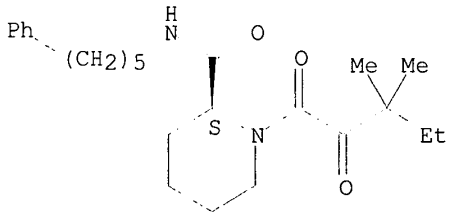
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxamide, 1-(3,3-dimethyl-1,2-dioxopentyl)-N-(5-phenylpentyl)-, (2S)- (9CI)
MF C24 H36 N2 O3

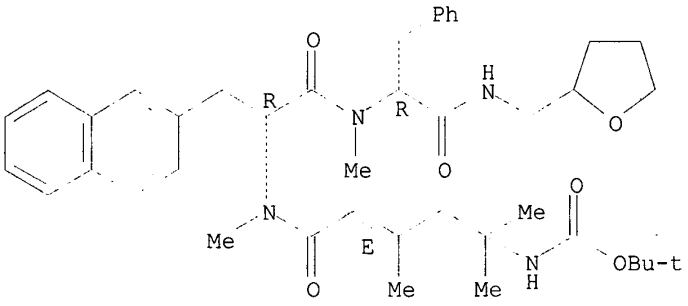
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Phenylalaninamide, N-[(2E)-5-[[(1,1-dimethylethoxy)carbonyl]amino]-3,5-dimethyl-1-oxo-2-hexenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N.alpha.-methyl-N-[(tetrahydro-2-furanyl)methyl]- (9CI)
MF C42 H56 N4 O6

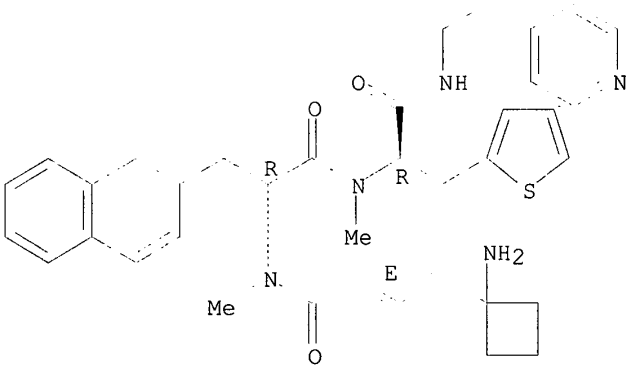
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Alaninamide, N-[(2E)-4-(1-aminocyclobutyl)-1-oxo-2-butenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N2-methyl-N-[2-(4-pyridinyl)ethyl]-3-(2-thienyl)- (9CI)
MF C37 H43 N5 O3 S

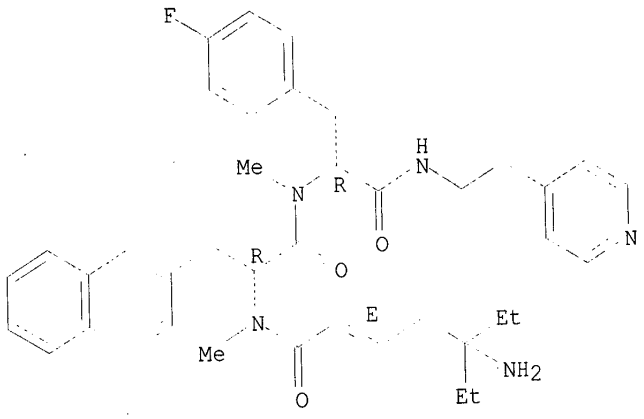
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Phenylalaninamide, N-[(2E)-5-amino-5-ethyl-1-oxo-2-heptenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-4-fluoro-N.alpha.-methyl-N-[2-(4-pyridinyl)ethyl]- (9CI)
MF C40 H48 F N5 O3

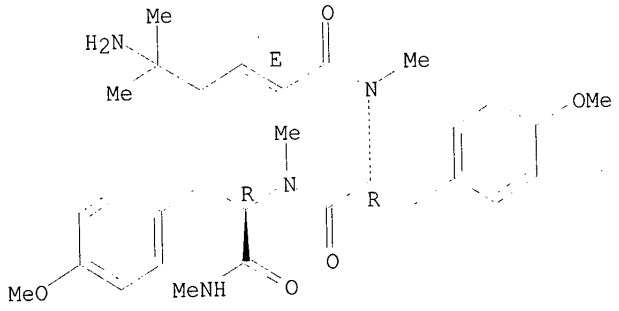
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN D-Tyrosinamide, N-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-N,O-dimethyl-D-tyrosyl-N,N.alpha.,O-trimethyl- (9CI)
MF C30 H42 N4 O5

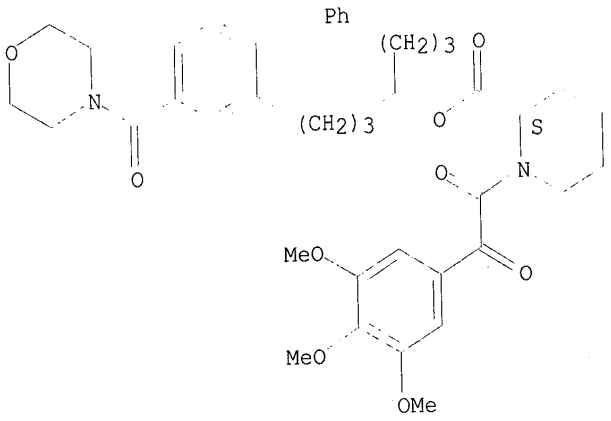
Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-[3-(4-morpholinylcarbonyl)phenyl]-1-(3-phenylpropyl)butyl ester, (2S)- (9CI)
MF C41 H50 N2 O9

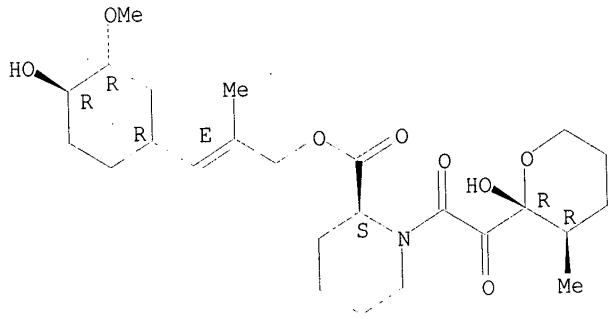
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L146 787 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Piperidinecarboxylic acid, 1-[oxo(tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl)acetyl]-, 3-(4-hydroxy-3-methoxycyclohexyl)-2-methyl-2-propenyl ester, [1R-[1.alpha.[E[S*(2R*,3R*)]],3.alpha.,4.beta.]]- (9CI)
MF C25 H39 N O8

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 08:15:03 ON 08 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    7 APR 2003  HIGHEST RN 502131-66-0
DICTIONARY FILE UPDATES:   7 APR 2003  HIGHEST RN 502131-66-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d sta que l40
L38                 STR
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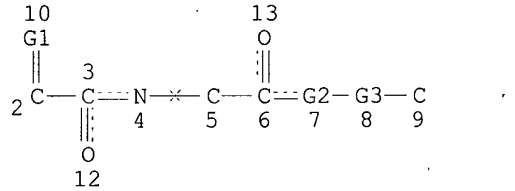


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VAR G2=CH2/O/N
REP G3=(0-3) CH2
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
L40       14064 SEA FILE=REGISTRY SSS FUL L38

100.0% PROCESSED 247016 ITERATIONS                      14064 ANSWERS
SEARCH TIME: 00.00.02


=> d his

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               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 06:53:18 ON 08 APR 2003
               E ROTAMASE/CN
L1             1 S E3
               E ROTAMASE
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L2           40 S E3
                SEL CHEM L1

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L4          998 S L2
                E ROTAMASE
L5          173 S E3-E5
L6         1411 S L3-L5
                E IMMUNOPHILIN/CT
L7          100 S E7-E10
                E E5+ALL
L8         1948 S E3,E2+NT
L9          958 S IMMUNOPHILIN?
L10        1348 S (FK506 OR FK 506)(L)(BP OR BINDING PROTEIN)
L11        1559 S FKBP?
L12        2788 S L7-L11
                E STEINER J/AU
L13          63 S E3,E13
                E STEINER JOE/AU
L14           3 S E3
L15         114 S E22,E24,E25
                E HAMILTON G/AU
L16          64 S E3,E17,E18
                E HAMILTON GREG/AU
L17         136 S E3-E6,E9,E10
                E GUILFORD/PA,CS
                E GUILF/PA,CS
L18         430 S E5-E40
L19         427 S GUILFORD?/PA,CS
L20           6 S (US6509477 OR US5614547)/PN
L21           4 S (US20020052410 OR US20020013344)/PN
                E GPI/PA,CS
L22          26 S E20-E23
L23         116 S L13-L22 AND L3-L12
L24           8 S L20,L21 AND L23
L25         340 S PEPTIDYL PROLYL ISOMERASE
L26          36 S L25 AND L13-L23
L27           4 S L24 AND L26
L28           8 S L24,L27
L29         108 S L23,L26 NOT L28
L30        3504 S L6,L12,L25

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L32          199 S L31

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L33          SEL L29 1- RN :    1566 TERMS
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